EXHIBIT 3

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LIGITATION	**Master File No. 2:12-MD-02327** **MDL No. 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO PLAINTIFFS: **Carolyn Lewis (2:12-cv-04301)** **Judy Brown (2:12-cv-07314)**	

RULE 26 EXPERT REPORT OF BRUCE ROSENZWEIG, M.D.

I. Qualifications

I am currently an Assistant Professor of Obstetrics and Gynecology at Rush University Medical Center in Chicago, Illinois. I received my MD degree in 1984 from the University of Michigan in Ann Arbor, Michigan. Following graduation from medical school, I completed an Obstetrics and Gynecology Residency at Michael Reese Hospital in Chicago. In 1988, I attended a one year pelvic surgery fellowship at State University of New York in Syracuse, New York. Following that fellowship, I attended a two year Urogynecology and Urodynamics fellowship at UCLA Harbor General Hospital in Torrance, California. After graduating from the Urogynecology fellowship, I became a faculty member at the University of Illinois in Chicago. I started a Urogynecology program at the University of Illinois and also was the residency program director.

In 1998, I went into private practice, and subsequently established a private practice at Rush University Medical Center. I have also worked at John H. Stroger Hospital here in Chicago from May 2003 until November 2010 and Weiss Memorial Hospital as Associate Chair of Gynecology from February 2011 until July 2012. I have published numerous articles and given numerous lectures on the topics of pelvic organ prolapse, urinary incontinence and repair of pelvic organ prolapse.

Throughout my career, I have performed over a thousand pelvic floor surgical procedures, including abdominal sacrocolpopexy, uterosacral suspensions, sacrospinous ligament fixations, native tissue repairs, biological graft repairs and synthetic mesh repairs. I have also used numerous synthetic pelvic mesh products, including Ethicon's TVT, TVT-Obturator, and Prolift. In addition, I have performed over 200 surgeries dealing with complications related to synthetic mesh, including the removal of numerous TVT devices.

I was also invited by Ethicon and attended both its Gynecare Prolift Training Seminar and TVT Obturator Seminar in Belgium. In addition, I was also invited and attended a Bard Avaulta training seminar.

A copy of my CV and Fee Schedule is attached as Exhibit "A" and a copy of my testimony for the last four years is attached as Exhibit "B". The documents I relied on for this report are contained in Exhibit "C" as well as those documents cited throughout this Report.

I. Summary of Opinions

In formulating my opinions and preparing this report, I reviewed scientific literature, corporate documents from Ethicon, sample products and depositions of Ethicon employees. The corporate documents, sample products and depositions were supplied to me by counsel. A list of

Ethicon corporate documents and depositions reviewed for this report is attached hereto as Exhibit "B"; all other materials reviewed are listed at the end of this report. All opinions I have are to a reasonable degree of medical and scientific certainty. I understand discovery is still ongoing in this case and I reserve my right to amend my opinions if further information is provided in any form including, but not limited to corporate documents, depositions and the expert reports of both Plaintiff and Defense experts.

In general, my expert opinions can be summarized as follows[1]:

A) Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence because it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, roping and curling of the mesh, and loss of pore size with tension;

B) Ethicon's Disclosures of Adverse Reactions and mesh complications in its TVT Instructions for Use ("IFU") were inadequate based on the adverse eactions/risks and mesh complications known to Ethicon from the time the TVT was first sold and marketed until present day;

C) Ethicon did not disclose information to physicians in its IFUs regarding characteristics of the polypropylene in Ethicon's TVT mesh (Prolene) that make it unsuitable for its intended application as a permanent prosthetic implant for stress urinary incontinence, including that it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, roping and curling of the mesh., and loss of pore size with tension;

D) Ethicon failed to adequately describe, inform or explain to physicians how to properly "tension" the TVT and inform them that improper tension on the mesh decreased effective pore size and interfered with incorporation into tissue;

E) Ethicon did not inform physicians and their patients that Manufacturer Safety Data Sheets (MSDSs) for polypropylene resin used to manufacturer polypropylene meshes warned against use of the mesh in a permanently implanted medical device and that studies showed that it caused sarcomas in laboratory rats;

F) Ethicon did not properly inform physicians and their patients that toxicity testing of the polypropylene mesh revealed that it was cytotoxic; ;

[1] This is not intended to be an exhaustive recitation of my opinions in this case. The full scope of my opinions are described in further detail in this report.

G) Ethicon's promotional materials sent to physicians related to TVT were inaccurate and failed to reveal material facts about complications and conflict of interests regarding data promoted in the materials;

H) Ethicon's Patient Brochures misstate information regarding complications and success rates and overstate the benefits of the TVT and understate the risks .

II. Background and Treatment Options for Stress Urinary Incontinence

1. Stress Urinary Incontinence

Approximately one of three women over the age of 45 years old have some form of urinary incontinence. The majority of those women do not seek medical advice or treatment for a variety of reasons.

In a continent individual, increased abdominal pressure is evenly distributed over the bladder, bladder neck, and urethra. The urethral sphincter is thus able to withstand this pressure and maintain continence. In a person with pure stress urinary incontinence, either the urethra is hypermobile or the sphincter is intrinsically deficient. In urethral hypermobility, the urethrovesical junction (UVJ) is displaced extra-abdominally, and the increased intra-abdominal pressure is unevenly distributed such that the sphincter can no longer withstand the pressure and urine leaks. With intrinsic sphincter deficiency (ISD), the UVJ is not hypermobile; however, the maximal urethral closing pressure, the Valsalva leak-point pressure, or both are too low to withstand the increase in intra-abdominal pressure and, thus, urine leaks past the sphincter

Stress urinary incontinence (SUI) is the involuntary leakage of urine during moments of physical activity that increases abdominal pressure, such as coughing, sneezing, laughing, or exercise, in the absence of a bladder contraction. It has been estimated that 14% of women have SUI. SUI is a common type of urinary incontinence in women. Urodynamic proven SUI is

found in approximately 50 % of women presenting for evaluation of urinary incontinence. Symptomatic women with SUI have social or hygienic consequence from their urine loss. SUI can happen when pelvic tissues and muscles, which support the bladder and urethra, become weak and allow the bladder "neck" (where the bladder and urethra intersect) to descend during bursts of physical activity (urethral hypermobility). This descent can prevent the urethra from working properly to control the flow of urine. SUI can also occur when the sphincter muscle that controls the urethra weakens(intrinsic sphincter deficiency). The weakened sphincter muscle is not able to stop the flow of urine under normal circumstances, and when there is an increase in abdominal pressure. Weakness may occur from pregnancy, childbirth, aging, or prior pelvic surgery. It has been estimate that a majority of women have a combination of urethral hypermobility and ISD. Other risk factors for SUI include chronic coughing or straining, constipation, obesity and smoking. Finally occult or latent SUI is defined as a positive stress test, loss of urine with increased intra-abdominal pressure and between 350-450cc volume in the bladder, after the repositioning of pelvic organ prolapse (usually accomplished with a ring pessary carefully positioned as to avoid compression of the urethra) in an otherwise clinically continent patient.

2. Nonsurgical Treatment of SUI

There are numerous non-surgical treatments available to woman with SUI. First, Pelvic Floor Exercises**:** A type of exercise to strengthen the pelvic floor by contracting and relaxing the levator muscles that surround the opening of the urethra, vagina, and rectum. These exercises, commonly referred to as Kegel exercises, improve the pelvic floor muscles' strength and

function. Kegel exercises can improve over-active bladders by increasing urethral resistance with can trigger the bladder to relax.

Second, Pessary**:** A removable device that is inserted into the vagina against the vaginal wall and urethra to support the bladder neck. This helps reposition the urethra to reduce SUI. These can be made of rubber, latex or silicon. Inserted into the vagina, a pessary rests against the back of the pubic bone and supports the bladder. Pessaries are available in various forms, including donut and cube shapes, and must be fitted by a healthcare provider. Some women who have stress incontinence use a pessary just during activities that are likely to cause urine leakage, such as jogging. Special incontinence pessaries have a 'knob', which fits under the urethra to elevate the midurethra to prevent urine loss.

Third, Transurethral Bulking Agents: Bulking agent injections are applied around the urethra that make the space around the urethra thicker, thus helping to control urine leakage. The effects are usually notpermanent.

Fourth, Behavioral Modification**:** This includes avoiding activities that trigger episodes of leaking. Lifestyle modification can improve stress incontinence symptoms and include quitting smoking, weight loss, and allergy treatment during seasonal allergies.

Fifth, Urinary seals**:** These are adhesive foam pads, which women place over the urethral opening. The pad creates a seal and prevents the leakage of urine, providing incontinence treatment. The pad is removed before urination and replaced with a new one afterward. The pad can be worn during exercise or physical activity, but not during sexual intercourse.

Sixth, Urethral insert**:** A thin, flexible tube that is solid rather than hollow (like a catheter) is placed into the urethra to block the leakage of urine These small plugs are inserted into the urethra by women to prevent leakage, and are removed prior to urination. These inserts can be uncomfortable and may increase the risk of urinary tract infection.

Seventh, Bladder neck support device**:** This device is a flexible ring with two ridges. Once inserted into the vagina, the ridges press against the vaginal walls and support the urethra. By lifting the bladder neck, it provides better bladder control in women suffering from stress incontinence. The device needs to be sized to fit, and must be removed and cleaned after urination. Bladder neck support devices can be uncomfortable and may cause urinary tract infections.

3. Surgical Treatment of SUI

a. The Burch Colposuspension

Retropubic approaches for the treatment of stress urinary incontinence include the Burch retropubic urethropexy (both open and laparoscopic) and the Marshall-Marchetti-Krantz (MMK) procedure. The goal of both of these procedures is to suspend and stabilize the urethra so that the urethrovesical junction (UVJ) and proximal urethra are replaced intra-abdominally and to recreate a firm backstop for intra-abdominal pressure. This anatomic placement allows normal pressure transmission during periods of increased intra-abdominal pressure restoring continence in a previously incontinent, hypermobile UVJ.

The Burch procedure was described in 1961. Initially, Burch described attaching the paravaginal fascia to the arcus tendineus. However, this was later changed the point of

attachment to Cooper's ligaments because these were felt to provide more secure fixation points, and less chance of infection as seen with the prior MMK procedure.

Patients with type III stress urinary incontinence (a fixed, nonfunctioning proximal urethra) are not ideal candidates for a Burch procedure as no hypermobility exists to correct.

For the Burch procedure, a low Pfannestiel incision is made above the pubic bone in order to enter the space of Retzius (the anatomical space between the pubic bone and the bladder above the peritonium in order to suspend the bladder and/or to perform a paravaginal repair. The procedure involves placing permanent stitches adjacent to the neck of the bladder and either proximal or distal to the bladder neck stitches on each side and suturing them Cooper's ligament which is attached to the pubic bone. The paravaginal repair is very similar except that the stitches are attached to the arcus tendentious linea pelvis. The likelihood of success of the Burch and the paravaginal repair procedures is reported to be 80-90% in most cases. Success means total elimination of the incontinence and patient satisfaction score greater than 90%. Improved means significant reduction of urine loss and greater than 70% improvement of patient satisfaction scores. Additionally, these retropubic procedures can be accomplished by the laparoscopic route. With respect to the selection of synthetic absorbable suture versus non-absorbable suture, and braided versus monofilament, no prospective randomized blinded data exist to suggest superiority of one suture material over another. However, recognized risks are associated with bone anchors. Modifications in the technique can be used if co-existent central defect cystocele is present and obliteration of the cul-de-sac can be performed to prevent enterocele or posterior vaginal wall prolapse after Burch colposuspension.

b. Pubovaginal sling procedures

Pubovaginal slings have excellent overall success and durable cure. The procedure involves placing a band of autologous, allograft, xenograft or synthetic material directly under the bladder neck (ie, proximal urethra) or mid-urethra, which acts as a physical support to prevent bladder neck and urethral descent during physical activity. This is brought up through the rectus fascia. The sling also may augment the resting urethral closure pressure with increases in intra-abdominal pressure.

Von Giordano is usually credited with performing the first pubovaginal sling operation in 1907, using a gracilis muscle graft around the urethra. In 1914, Frangenheim used rectus abdominis muscle and fascia for pubovaginal slings. In 1942, Aldridge, Millin, and Read corrected urinary incontinence using fascial slings. In 1965, Zoedler and Boeminghous first introduced synthetic slings.

Historically, surgeons have used the fascia lata sling for recurrent SUI after a failed anti-incontinence operation. Furthermore, this operation is used extensively for the treatment of primary ISD. If the abdominal tissues are weak and attenuated or if the vaginal tissues are atrophied or in short supply, constructing a pubovaginal sling from the leg fascia lata can be performed. This procedure is more involved than the creation of the rectus fascial sling as it requires a second incision to harvest the fascia lata and healing in an area remote for the index procedure.

An alternative to a long rectus sling is construction of a short sling from a much smaller piece of abdominal fascia (rectus fascia suburethral sling). The surgical procedure is similar to that used for the rectus fascia pubovaginal sling, except that the harvested fascial tissue is much smaller and the operation time shorter. The advantage of this procedure is its simplicity. No

extensive dissection in the suprapubic area is necessary, and the postoperative result is similar to that of the full-length fascial strip sling.

An alternative to a long fascia lata sling is the use of a postage stamp–sized patch of fascia lata from the outer thigh (fascia lata suburethral sling). The surgical procedure is similar to that for the fascia lata pubovaginal sling, except the harvested fascia is much smaller. This operation does not require extensive dissection in the thigh area, and the postoperative result is similar to that of the full-length fascia lata strip sling. Postoperative convalescence is shorter than that of the fascia lata pubovaginal sling procedure.

The vaginal wall suburethral sling helps restore urethral resistance by increasing urethral compression and improving mucosal coaptation of the bladder neck. This operation is attractive because it is simple and easy to perform. Postoperative complications are minimal, and the recuperative period is short. Vaginal sling surgery is relatively contraindicated in elderly women with atrophic vaginitis. If recognized before surgery, the atrophied vaginal wall may be revitalized with the administration of vaginal estrogen cream or tablets for 3-6 months.

A clear contraindication to pubovaginal sling surgery is pure urge incontinence or mixed urinary incontinence (MUI) in which urge is the predominant component. An inherent risk of any sling procedure is de novo or worsening urge symptoms; thus, surgeons must identify and treat the presence of an urge component before surgery.

Conversely, poor detrusor function is a relative contraindication to pubovaginal sling surgery because the potential for urinary retention is increased. Women with absent or poor

detrusor function in the presence of SUI are at a higher risk of experiencing prolonged postoperative urinary retention.

c. The Marshall-Marchetti-Krantz Procedure

The Marshall-Marchetti-Krantz procedure surgically reinforces the bladder neck in order to prevent unintentional urine loss. For the Marshall-Marchetti-Krantz procedure an incision is made similar to that for the Burch procedure. The bladder is separated from surrounding tissues. Sutures are placed at the level of the midurethra and bladder neck through the vaginal fascia and then brought up to the symphysis pubis.

d. Midurethral Synthetic Slings

Based on the "Integral theory of female incontinence," Prof. Ulmsten developed a midurethral procedure to treat stress urinary incontinence. The first reports of this procedure appeared in 1996 as an intravaginal slingoplasty. The "tape'" was place through a small vaginal incision at the midurethra, brought through the urogenital diaphragm through the retropubic space and exited through small suprapubic incisions. The operation was theorized to correct incontinence by recreating the midurethral support of the pubourethral ligament and also by creating a midurethral hammock for support of the urethra during stress events. The procedure was described to have a success rate of 85-90% with an additional 5-10% significantly improved. The Gynecare TVT system was introduced in the US in November of 1998. Early studies showed that the risk of bladder perforation during the procedure occurred 5-10% of cases and vascular injury with /without hematoma formation occurred in 2-5% of patients.

In an attempt to decrease the risk of bladder perforation and vascular injury, a 'top-down' approach to trocar placement was promoted as the SPARC procedure, introduced in the US in 2001 by American Medical Systems (AMS). The next modification of the midurethral sling came in 2001 when Delorme described his results for the use of the obturator membrane and inner thigh for passage of the sling material. The proposed advantage was avoidance of the retropubic space, thus avoiding bladder perforation and retropubic vascular injury. The trocars were passed from the inner thigh through the obturator membrane from an "outside – in direction".

The next modification came from de Leval in 2003, with the "inside-out" trocar placement for the transobturator sling. The FDA's Executive Summary 2011 found less mesh vaginal erosion in transobturator vs TVT (1.3%) vs (1.9%), less bladder perforation (0.3%) vs (5.5%), and less voiding dysfunction (4%) vs (7%), but a higher rate of groin pain (12%) vs (1.7%). Similar efficacy has been demonstrated for the transobturator vs retropubic approach.

The final modification came around 2006 with the release of the mini-slings, or single incision slings, which use support devices at the ends of shorter mesh lengths to accomplish fixation without the need for a secondary cutaneous exit point. The mini-slings could be placed in a retropubic or "U" fashion or a hammock or "H" fashion.

The FDA concluded in 2011 that there was higher peri-operative blood loss, higher mesh exposure and greater need for surgical re-intervention in the TVT-Secur (mini-sling) patients.

III. Expert Opinions

A. Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence because it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, roping and curling of the mesh, and loss of pore size with tension.

Polypropylene mesh (Prolene) like that contained in the TVT has many well-known characteristics that should have caused Ethicon to avoid its use in a product intended for permanent implantation into the human vaginal floor. These characteristics include the following: (1) degradation of the mesh; (2) chronic foreign body reaction; (3) fraying and particle loss; (4) Infections and Bio-films; (5) roping and curling of the mesh; (6) loss of pore size with tension; (7) fibrotic bridging leading to scar plate formation and mesh encapsulation; and (8) shrinkage/contraction of the encapsulated mesh.

As a result of these and other inadequacies with the mesh, and for the reasons set forth below, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT causes a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

1. The Prolene Mesh in TVT Degrades Over Time

The placement of permanent polypropylene mesh in the human vagina creates problems because of the chemical composition and structure of the mesh and the physiological conditions of the vagina and the surrounding tissues. There have been numerous studies over the last 30 years which have shown polypropylene to be chemically reactive and not inert, with flaking and fissuring demonstrated by scanning electron microscopy, which leads to degradation and release of toxic compounds into pelvic tissues. This process enhances the inflammatory and fibrotic reactions within the tissues in the pelvic floor, causing a multitude of problems.[2] There have been recent studies suggesting that oxidation of the mesh occurs because of the polypropylene and the conditions in which it is placed.[3] The oxidation causes the mesh to degrade, crack and break apart.[4] In another recent study, 100 pelvic mesh implants were compared and over 20% showed degradation to mesh fibers.[5]

Because of the structural complexities of the vagina and the nature of the chemicals ordinarily found in the vagina and its surrounding tissues**,** there are several reasons why polypropylene presents unique problems when placed in the vagina. An Engineering Bulletin from Propex, entitled "EB-405, The Durability of Polypropylene Geotextiles for Waste Containment Application," from 2011, states that, "[P]olypropylene is vulnerable to the following substances: highly oxidized substances such as (peroxide), certain chlorinated

[2] Coda A, Hernia 2003;7:29; Jongebloed, WL, "Degradation of Polypropylene in the Human Eye: A SEM Study," Doc Ophthalmol., 1986 64(1:143-152); Skrypunch, OW, "Giant Papillary Conjunctivitis from an Exposed Prolene Suture," Can J Ophthalmology, 198621:(5: 189-192).

[3] Costello C, Bachman S, Grant S, Cleveland D, Loy T, Ramshaw B, "Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient," Surgical Innovation , 2007, 143: 168-176).

[4] Id.

[5] Clavé A, Yahi H, Hammou JC, Montanari S, Gounon P, Clavé H, "Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants,: J Biomed Mater Res B Appl Biomater, 2007, Oct 83(1:44-9).

hydrocarbons (halogenated hydrocarbons), and certain aromatic hydrocarbons."[6] It is well known to physicians with expertise in the pelvic floor that vaginal and perivaginal tissues are ready sources for peroxide. The vaginal species lactobacillus produces hydrogen peroxide and lactic acid from collagen that is produced in the squamous cells of the vagina. Estrogen is the catalyst for the production of glycogen from the vaginal cells. It is also well known that hydrogen peroxide produced by the lactobacillus species is important in controlling the vaginal micro-flora. In fact, the vagina is a ready source of hydrogen peroxide production. In a manuscript from M Strus, "The In Vitro Effects of Hydrogen Peroxide on Vaginal Microbial Communities," the authors show the amount of hydrogen peroxide produced by the lactobacillus species.[7] "Hydrogen Peroxide reached concentrations of from 0.05 to 1.0 mM, which under intensive aeration increases even up to 1.8 mM."[8] These results confirmed the previous results of M Strus in the publication, "Hydrogen Peroxide Produced by Lactobacillus Species as a Regulatory Molecule for Vaginal Micro-flora," Med Dosw Microbiol, 2004: 56(1:67-77).

It is also known that aromatic hydrocarbons can be found in the human body. In a paper from HB Moon entitled, "Occurrence and Accumulation Patterns of Polycyclic Aromatic Hydrocarbons and Synthetic Musk Compounds in Adipose Tissues of Korean Females," *Chemosphere* 2012 (86:485-490), these aromatic hydrocarbons were noted to be present in, "[t]otal concentrations of PAHs and SMCs in adipose tissues rang[ing] from 15 to 361 (mean:119) ngg(-1) lipid weight and from 38 to 253 (mean:106) nng(-1) lipid weight

[6] Citing Schneider H., Long Term Performance of Polypropylene Geosynthetics," Durability and Aging of Geosynthetics, Koerner, RM, Ed., (Elsevier 1989) 95-109.

[7] Strus, M, et al., "The In Vitro Effect of Hydrgen Peroxide in Vaginal Microbial Communities," FEMS Immunol Med Microbiol, 2006 Oct; 48(1:56-63).

[8] Id.

respectively . . . . The results of this study provide baseline information on exposure of PAHs and SMCs to the general population in Koreans."

It has also been determined that halogenated hydrocarbons can be found not only in adipose tissue but also the blood stream. A paper entitled, "Determination of Volatile Purgeable Halogenated Hydrocarbon in Human Adipose Tissue and Blood Stream," from the *Bulletin of Environmental Contamination and Toxicology*, Volume 23, Issue 1, pp 244 – 249 published in 1979, found halogenated hydrocarbons, pesticide by-products, both in human adipose tissues and the blood stream. In a subsequent paper from 1985 in *Environmental Health Perspectives*, Voloume 60, pp. 127-131, Henry Anderson, in his paper entitled, "Utilization of Adipose Tissue Biopsy and Characterizing Human Halogenated Hydrocarbon Exposure," also found these pesticide by-products in human adipose tissue.

Accordingly, the body location where the polypropylene mesh is being placed can expose it to known chemical degradation agents However, chemical degradation is not the only way that polypropylene degrades in vivo. In a paper from N Das in the *Journal of Biotechnology Research International*, Volume 2011, Article ID 941810, entitled, "Review Article: Microbial Degradation of Petroleum Hydrocarbons Contaminant: An Overview," found that various bacteria such as Pseudomonas species, Bacillus species, Mycobacterium and Corynebacterium species, which are present in a woman's vagina, can degrade petroleum hydrocarbons. Also fungi such as the Candida species, also present, can degrade petroleum-based hydrocarbons.[9]

Microbial agents that can be found inside the normal and abnormal flora of the human vagina such as Candida and, with certain pelvic infections such as Bacillus and Pseudomonas, can be a source of biological degradation of polypropylene products. A paper entitled, "Health,

[9] Das, N , et al., "Review Article: Microbial Degradadtion of Petroleum Hydrocarbon Contaminants: an Overview," J Biotech Res Intl, 2011, Article ID 941810, 1-13.

Safety and Environment Fact Sheet: Hazardous Substances - Plastics," from CAW/TCA (www.caw.ca), August 2011:343, found that polypropylene degradation products and residues can form carbon monoxide, acrolein, aldehydes and acids, qualifying these health hazards as toxic and irritants. In a paper from D Lithner in 2011 at 4, entitled, "Environmental and Health Hazards of Chemicals in Plastic Polymers and Products",University of Gothenburg, it is stated that, "[n]on-biodegradable polymers can be degraded by heat, oxidation, light, ionic radiation, hydrolysis and mechanical shear, and by pollutants such as carbon monoxide, sulphur dioxide, nitrogen oxide and ozone. This causes the polymer to get brittle, to fragment into small pieces and to release degradation products." (Citations omitted.) She continues, "[o]ther substances (besides monomers) are often needed for polymerization to occur, for instance initiators, catalysts, and, depending on manufacturing process, solvents may also be used. The resulting plastic polymer can be blended with different additives, for instance plasticizers, flame retardants, heat stabilizers, antioxidants, light stabilizers, lubricants, acid scavengers, antimicrobial agents, anti-static agents, pigments, blowing agents and fillers, and is finally processed into a plastic product. There are many different plastic polymers and several thousand different additives, which result in an extremely large variation in chemical composition of plastic products." Id. at 6 (citations omitted). "Since plastic products are composed of many different chemicals, and the main part of these [are] broken down into something completely different; this complicates the prediction." Id. at 8. "The type and quantity of degradation products formed may also be influenced by degradation mechanisms, presence of polymerization impurities, and surrounding factors, e.g. temperature and oxygen." Id. at 9. "Few studies combining leaching tests with toxicity tests have been performed on plastic products." Id. at 12.

The available peer-reviewed literature regarding degradation/oxidation of polypropylene in the human body dates back to the 1960's and has been reported in numerous such publications. [10] Two of the more important and salient articles regarding reported degradation in explanted surgical meshes (hernia and pelvic floor) are the Costello and Clave articles.

In his paper, "Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Implants from a Single Patient,'' Prof. C Costello reported that hernia mesh made of polypropylene oxidized and degraded as a result of the metabolites produced by phagocytic cells during the body's inflammatory reaction to the mesh. High-magnification photographs showed cracking and peeling of the polypropylene fibers. Ethicon was aware of this article as referenced in internal emails.[11]

Another article by A Clave, "Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants," also displayed high magnification photos of polypropylene fibers from explanted meshes and, in this case, the meshes were explanted from women's pelvic floor tissue. *International Urogynecology Journal*, 2010 (21:261-270). The heavyweight meshes showed even greater cracking than the lower density meshes, but according to Prof/Dr. Clave, ALL 84 of the polypropylene explants examined showed degradation. Oxidation of the implanted mesh due to free radical attack through the synthesis of peroxides, superoxides and hypochlorous acid during the chronic inflammatory phase was listed as just one potential cause for the oxidative degradation within the "septic environment" in which the pelvic meshes are placed.

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[10] Liebert T, Chartoff R, Costgrove S, "Subcutaneous Implants of Polypropylene Filaments," J Biomed Mater Res. 1976 (10:939-951); Williams D, "Review of Biodegradation of Surgical Polymers,". J Materials Sci, 1982 (17:1233-1246); Oswald, HJ, Turi, E, "The Deterioration of Polypropylene By Oxidative Degradation," Polymer Eng Sci, 1965 (5:152-158).

[11] Eth.Mesh.005588123

Given the information available to Ethicon in the scientific and medical literature concerning the potential for degradation of polypropylene, it is my opinion to a reasonable degree of medical certainty that Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's body's would react differently to the mesh and the degradative process and its by-products.

This is especially true given the fact that Ethicon knew degradation of its mesh could occur. As seen in testimony from Daniel Burkley, Principal Scientist at Ethicon, Ethicon was aware that mesh could shrink, contract and degrade. Specifically, Mr. Burkley agreed that the risk of degradation increases when you have a severe inflammatory response with mesh implanted in a contaminated field.[12] Mr. Burkley also testified that polypropylene mesh in human beings is subject to some slight degree of surface degradation.[13] He agreed that degradation might be better understood if Ethicon studied or tested a product that is permanently implanted in women.[14]

In fact, according to Mr. Burkley, Ethicon only conducted one study related to degradation and Prolene material. This study consisted of a Prolene suture implanted into dogs.[15] Mr. Burkley testified that the study and photos from the dog actually showed that the Prolene material used in TVT degraded and was still degrading after 7 years.[16]

[12] Burkley 5/22/13 184:17-24.
[13] Burkley 5/22/13206:2-11.
[14] Burkley 5/22/13 206:12-25.
[15] Eth.Mesh.05453719 (Seven year data for ten year Prolene study: ERF 85-219)
[16] Burkley 5/23/13 315:8-13.

Ethicon hired an outside consulting firm to resolve the cause of the erosion of its surgical meshes for the pelvic floor. In a June 22, 2011 report, PA Consulting Group informed Ethicon that, "[p]olypropylene can suffer from degradation following implant . . . a process which initiates after a few days post implantation in animal studies."[17] The consulting report discusses numerous images of polypropylene mesh that show "physical degradation" of the mesh. [18] In addition, in a 2009 presentation, Ethicon Medical Director Piet Hinoul states that meshes are not biologically inert.[19]

I have reviewed the report of Dr. Howard Jordi, an expert in this litigation, regarding his lab's testing of six TVT and TVT-O control samples against 22 explanted meshes. Dr. Jordi's findings and test results further support my opinions regarding the degradation of Ethicon's TVT meshes in a woman's pelvic tissues. I have reviewed the numerous microscopic photos taken of explanted Prolene mesh from TVT and TVT-O in Dr. Jordi's report which show degradation of the mesh. These photos further support my opinion regarding the degradation of the Prolene mesh. Further, as stated in Dr. Jordi's report, the two anti-oxidants that Ethicon adds to its Prolene mesh used in TVT was present in the control samples but virtually absent in the explant specimens. As such, without anti-oxidants to protect the polypropylene in vivo, there is a significantly increased risk of oxidation/degradation in a woman's pelvic tissues after implantation of TVT mesh.

Interestingly, despite years of the scientific literature, its own internal dog study and reports from consultants it hired that state degradation of the mesh occurs, Ethicon's Instructions for Use (IFU) continues to claim to this day that the mesh in the TVT, "is not absorbed, nor is it

[17] Eth.Mesh.02589032 and Eth.Mesh.07192929 (May 18, 2011 PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentation).
[18] Id.
[19] Eth.Mesh.01264260 (Presentation, "Prolift+M," P Hinoul, MD, Ethicon Pelvic Floor Expert's Meeting – Nederland,Utrecht, May 7, 2009).

subject to degradation or weakening by the action of enzymes."[20] This is not simply inaccurate, but is false and misleading for all of the reasons stated above, including, most importantly, that Ethicon's own internal documents and testimony from its employees confirm that the TVT degrades.

It is my opinion to a reasonable degree of medical certainty that the effect of chemical and biological degradation of the TVT Prolene mesh in a woman's tissues can lead to a greater foreign body reaction, enhanced inflammatory response and excessive scarring, which can lead to severe complications in patients, including the including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

2. Chronic Foreign Body Reaction

The human body has a natural and fairly predictable "host defense response" to any foreign object placed inside of it. Whether a splinter or a surgical mesh, the human body will send white blood cells to attack the invader and, if the products of inflammation cannot ward off

[20] Eth.Mesh.05225354; Eth.Mesh.02340306; Eth.Mesh.02340471; Eth.Mesh.05222673; Eth.Mesh.02340504; Eth.Mesh.03427878.

or destroy the invader, including the invader is anything from bacteria to prosthetic implants, the initial acute inflammatory phases is followed by a chronic inflammatory phase. Therefore, with the placement of something like a permanent surgical mesh in human tissues, there will be a chronic or permanent foreign body reaction to the implant, as well as a chronic inflammatory response by the body. [21] In fact, Ethicon Medical Directors, Piet Hinoul and Charlotte Owens, have both testified that the chronic foreign body reaction created by the body's response to mesh can cause a severe inflammatory reaction, which can cause chronic pain, nerve entrapment, erosions, dyspareunia and the need for additional surgeries.[22]

Ethicon was informed by its consultants and experts in the field that there will be chronic tissue reaction to its polypropylene meshes. During a 2006 meeting at one of Ethicon's facilities, Bernd Klosterhalfen, a pathology consultant expert for Ethicon, informed Ethicon that there can be a continuing reaction between tissues in the body and mesh for up to 20 years.[23] In addition, during a February 2007 meeting, Ethicon stated that there can be, "[E]xcessive FBR [foreign body reaction]> massive scar plate > more shrinkage."[24] As discussed above, Ethicon is clearly aware that its TVT mesh can cause a foreign body reaction which cascades into a multitude of problems leading to injuries for the women in whom it is implanted. This is best seen in the testimony of Ethicon Scientist, Joerg Holste.[25] Dr. Holste testified that chronic foreign body reactions occurs in Ethicon's small pore, heavyweight meshes like the Prolene mesh found in

[21] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V, "Shrinking of Polypropylene Mesh In Vivo: An Experimental Study in Dogs,". Eur J Surg 1998 (164: 965-969); Klinge U, Klosterhalfen B, Muller M, Schumpelick V, "Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias,"; Eur J Surg, 1998 (164:951–960); Klostherhalfen,B, Junge, K, Klinge, U, "The lightweight and large porous mesh concept for hernia repair," Expert Rev. Med. Devices, 2005 2(1); Binnebosel M, von Trotha K, Jansen P, Conze J, Neumann U, Junge K, "Biocompatibility of prosthetic meshes in abdominal surgery" Semin Immunopathol, 2011 (33:235-243); Eth.Mesh.03658577 (Biocompatibility of Ultrapro).

[22] Hinoul 4/5/12 99 09-99:25; 4/6/12 518:14-520:20; 6/26/13 175:1-176:17,;184:18-22; and 328:10-24; Owens 9/12/2012 98:11-99:07.
[23] Eth.Mesh.00870466 (June 6, 2006 Ethicon Expert Meeting Meshes for Pelvic Floor Repair, Norderstedt).
[24] Eth.Mesh.01218361 (Ethicon Presentation: "State of Knowledge in 'mesh shrinkage'-What do we know").
[25] Holste 7/29/13 52:5-55:21.

TVT. In fact, Dr. Holste testified that Ethicon developed lighter weight, large pore meshes in order to minimize the complications seen with heavyweight meshes like the Prolene used in TVT. [26] Ethicon employee, Christophe Vailhe, testified that there can be an excessive inflammatory reaction or foreign body reaction that would lead to mesh erosion and contraction.[27] Despite its knowledge about the problems associated with chronic foreign body reaction, Ethicon continues to use a heavy weight, small pore mesh in its TVT product.

Ethicon informed doctors in its IFU that its TVT mesh was "non-reactive with a minimal and transient foreign body reaction."[28] This is true despite all of the internal documents and testimony discussed above from Ethicon's Medical Affairs and Research and Development employees that chronic foreign body reaction occurs in small pore, heavyweight meshes like the Prolene mesh in TVT.

For the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT creates a chronic foreign body reaction which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical

[26] Holste 7/29/13 51:3-53:6.
[27] Vailhe 6/21/13 383:8-19.
[28] Eth.Mesh.05225354; Eth.Mesh.02340306; Eth.Mesh.02340471; Eth.Mesh.05222673; Eth.Mesh.02340504; Eth.Mesh.03427878.

device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

3. Infections/Bio-films

The placement of midurethral slings, including TVT, violates one of the most basic tenets of surgical teachings in that it is the placement of a permanent implant into the human through a "clean contaminated" surgical field, i.e. the vagina, which is not sterile and can never be completely sterilized, Therefore, implantation through the vagina is contraindicated for every procedure and implantation.

In TVT, the weave of the mesh produces very small interstices which allow bacteria to enter and to hide from the host defenses designed to eliminate them. The bacteria can secrete anencasing polysaccharide slime (biofilm), which further serves to shield the bacteria from destruction by white blood cells and macrophages.[29] The effect and consequences of biofilm to increase the foreign body reaction, resulting in chronic infections, chronic inflammation, erosions, and mesh and scar contracture, was well known to Ethicon, as evidenced by the testimony of Ethicon's Head of Pre-Clinical, Dr. Joerg Holste.[30] Importantly, the biofilm actually serves as a protection for the bacteria surrounding the mesh fibers against the body's host defense response (white blood cells), which are intended to destroy foreign invaders like bacteria. Thus, the weave induces the creation of a shield against the body's defenses to the bacteria entrained in the woven mesh, inhibiting the body's ability to fight off the infective agents within the mesh.

[29] Osterberg B, et al., "Effect of Suture Materials on Bacterial Survival in Infected Wounds: An Experimental Study," Acta. Chir. Scand 1979 (145:7 431-434); Merritt K, "Factors Influencing Bacterial Adherence to Biomaterials," J Biomat Appl 1991 (5:185-203); An, Y, "Concise Review of Mechanisms of Bacterial Adhesion to Biomaterial Surfaces," J Biomed Mater Res (Appl Biomat), 1998 (43:338-348); The TVM Group: J. Berrocal, et al. Conceptual advances in the surgical management of genital prolapsed, J Gynecol Obsted Biol Reprod 2004: 33:577-587.

[30] Holste 7/30/13 295:24-298:14, 411:15-414:24.

The large surface area promotes wicking of fluids and bacteria and is a "bacterial super highway" which provides a safe haven for bacteria which attached themselves to the mesh during the insertion process.[31] Daniel Burkley testified that reducing surface area could reduce the amount of chronic inflammation.[32] Additionally, the size of the mesh placed equates to a large surface area with many places for bacteria to hide while being protected from host defenses leading to numerous complications.[33]

There have been numerous peer-reviewed journal articles regarding secondary-mesh related infections as well as the dangers of implanting surgical mesh in a clean/contaminated field. Of note, in May of this year, at the AUA meeting in San Diego, Dr.Shah and his colleagues reported on the "Bacteriological Analysis of Explanted Transvaginal Meshes," which included explanted samples of both SUI slings and prolapse meshes. Of the 50 explants examined, 52% of those explanted due to patient complaints' of painful mesh were infused with pathogenic organisms, 20% of those explanted due to vaginal erosions had pathogenic organism, and 83% of those explanted due to urinary tract erosions were contaminated with pathogenic organisms.[34]

When polypropylene particles separate from the surface of the mesh fiber due to degradation, see *infra*, Degradation, the surface area of the mesh is greatly increased thus providing even greater areas for bacterial adherence to the mesh, more elution of toxic compounds from the polypropylene, and also more of the free toxic polypropylene itself, all of

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[31] Klinge, U, et al., "Do Multifilament Alloplastic Meshes Increase the Infection Rate? Analysis of the Polymeric Surface, the Bacteria Adherence, and the In Vivo Consequences in a Rat Model," J Biomed Mater Res, 2002 (63:765-771); Vollebregt, A, et al., "Bacterial Colonisation of Collagen-Coated Polypropylene Vaginal Mesh: Are Additional Intraoperative Sterility Procedures Useful?" Int Urogyn J, 2009 (20:1345-51).

[32] Burkley 5/22/2013, 371.

[33] Klinge, supra, at n 26; Vollebregt, supra, n. 26.

[34] Shah, K., et al., Bateriological Analysis of Explanted Transvaginal Meshes (Abstract 1144)

which increases the inflammatory reaction and intensity of the fibrosis.[35] This cracking of the mesh surface also provides safe harbors for infectious bacteria to proliferate.

In his periodic histopathological analyses for Ethicon of its pelvic floor explants, Dr. Klosterhalfen reported to Ethicon that, in virtually 100% of those instances in which mesh had been explanted due to erosions, he found a secondary, mesh-related infection at the tissue/mesh interface.[36] Mesh exposure and erosion cause the fibers to be further exposed to bacteria that will adhere to and colonize on the mesh surface.

Ethicon employees have testified that they were aware of these biofilms forming on the surface of the mesh.[37] However, Ethicon never performed any long-term, clinical studies to determine whether the warnings given them through the peer-reviewed literature and by their own experts and consultants were accurate, namely that mesh-related infections are real; that they cause patient injury in the form mesh erosions and recurrent, late infections; and that the transvaginal implantation through and into the non-sterile, septic vagina is below the standard of care for any surgical technique, especially one used to treat non-life threatening conditions, such as stress urinary incontinence.

Therefore, it is my opinion to a reasonable degree of medical certainty that the TVT mesh is susceptible to biofilm formation due to the weave of the mesh allowing the infiltration, harboring, and protection of bacterial contaminants; the degraded mesh surface harboring bacteria; the passage through and into a clean/contaminated field; and after exposure/erosion of the mesh into the vagina or other organs, further contamination of the mesh with a multitude of vaginal flora that further increases the risk of harmful and recurrent infections in women.

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[35] Jongebloed, *supra*, n. 1; Sternschuss, G, Ostergard, DR, Patel H, "Post-Implantation Alterations of Polypropylene in the Human," J Urology, 2012 (188:27-32); Clave, *supra*, at 6.
[36] Eth.Mesh. 00006636
[37] Holste, 7/30/13, 283:19-284:5

Accordingly, the TVT transvaginal technique, as well as the TVT mesh itself, are not safe for their intended purpose of implantation into a woman's pelvic tissues and can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

Finally, Ethicon's claims in its IFU that the TVT mesh may "potentiate infection" is misleading, at best. If, by the intentionally ambiguous term, "potentiate", Ethicon means "cause", then this is false for all of the reasons stated above. If by "potentiate", Ethicon means "exacerbate an existing infection", then the statement is misleading at best. Ethicon had a duty to warn physicians in its IFU that a slimy, protective biofilm could form on the mesh leading to painful erosions, recurrent, late infections and the need for mesh removal. By not doing so, they did not adequately warn physicians about these important risks nor, by extension, provide surgeons with an opportunity to discuss these risks with their patients.

4. *Fibrotic Bridging*

Fibrotic bridging occurs when the fibers surrounding the pores of the mesh are too close together to allow the tissue in the pore enough room to recover from the trauma of tissue damage due to implanting a surgical prosthetic device. Pores that are large enough for good, newly-

vascularized tissue tend to be filled with fatty tissue versus small pores that become filled with scarred or fibrotic tissue. In those instances, the scar forms across the pores or "bridges" from one side of the pore to the other. This can occur either due to the granulomas around the mesh fibers joining together or due to densely-formed fibroblasts between these granulomas. Either way, such bridging can lead to the creation of a rigid, scar plate that can encapsulate the mesh with scar tissue. Simply put, small mesh pores that cause fibrotic bridging turn the mesh into a solid sheet of scar tissue and there is no space or room for tissue to grow into the mesh, which is the intended purpose of the mesh. The fibrotic bridging and scar plate prevents tissue in-growth and causes complications, including, among other things, pain with the rigid mesh, shrinkage, contraction of the mesh, erosions due to mechanical irritation in the tissue of a rigid, scar-plated mesh, nerve entrapment, chronic pain and dyspareunia.

It is clear from Ethicon internal documents that it was well aware of fibrotic bridging.[38] Ethicon employees have testified that the heavy weight, small pore type of mesh in the TVT can lead to an increased risk of foreign body reaction, contraction of the mesh, nerve entrapment, erosions and chronic pelvic pain.[39] This concept is best illustrated by a DVD produced by Ethicon which features an Ethicon consultant, Dr. Todd Henniford, talking about a heavy weight,

[38] Eth.Mesh.04037600 Innovations in mesh development; Eth.Mesh.05920616 7/20/07 ;Emails freom Chomiak, Martin to Batke, Boris; Jamieson, Gillian; Koehler, Petra; and Hellhammer, Dr. Brigitte, SUBJECT: Defining light weight mesh; TH.MESH.05585033 Boris Batke Presentation – Project Edelweis - Ultrapro; Eth.Mesh.05446127 3/13/2006 Emails from Holste, Dr. Joerg to Engel, Dr. Dieter; Manley, Quentin; Storch, Mark L. SUBJECT: AW: Mesh and Tissue Contraction in Animal – "Shrinking Meshes? – Scientific Statement by Ethicon GmbH, R&D Europe; Biocompatibility of Meshes by Dr. J. Holste; Eth.Mesh.05475773 2/09/2007 Boris Batke, Ethicon R&D, Presentation: The (clinical) argument of lightweight mesh in abdominal surgery; Eth.Mesh.04015102 3/01/12 Email from Batke, Boris to Mayes, Casey SUBJECT: AW: AGES Pelvic Floor Conference-Gala Dinner Invitation; Eth.Mesh.04037600 3/15/12 Boris, Batke PowerPoint Presentation, Innovations in Mesh Development, Melbourne AGES 2012.

[39] Batke 08/01/13 87:12 - 88:10, 113:3 - 114:3, 257:23 - 259:13; Holste 07/29/13 51:3- 53:6, 55:22 - 57:4; Vailhe 6/20/13 182:2 - 185:5.

small pore mesh called Marlex used for hernia repairs[40] Again, the Prolene mesh used in TVT is of heavyweight, small pore construction and, in fact, is even heavier than Marlex. Ethicon Scientists have acknowledged the video and that the Marlex mesh is similar to the Prolene in TVT in that is heavy weight small pore mesh.[41] In the video, Dr. Heniford talks about the dangers of heavy weight, small pore meshes.[42] In fact, Dr. Heniford states, "there is no excuse for using heavy weight, small pore meshes in the human body".[43] I have explanted numerous TVT meshes and have witnessed meshes with extensive scar plating and mesh encapsulation similar to the hardened/stiffened mesh viewed in the Heniford video.

In other emails, when discussing these concepts, Ethicon's World Wide Marketing Director for General Surgery, Marty Chomiak, states that "… we want to avoid 'bridging', therefore with think large pores are better than small . . ."[44]

Not only did Ethicon know about the problems with heavy weight, small pore mesh, it also had information and knowledge regarding superior mesh designs to prevent fibrotic bridging and scar plating. Specifically, Ethicon knew that light weight, large pore mesh could decrease the likelihood of foreign body reaction, fibrotic bridging and scar plating.[45] Despite its knowledge about the problems related to heavy weight, small pore mesh like the Prolene mesh and the problems it causes in pelvic tissues and patients, Ethicon has done nothing to change the

[40] B. Todd Heniford 2007 "The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair" Video produced by Ethicon.

[41] Eth.Mesh.05918776 5/04/04 Email from Schiaparelli, Jill, Strategic Grown Subject: Marlex Experience; Batke 08/01/13 87:12 - 88:10, 113:3 - 114:3, 257:23 - 259:13; Holste 07/29/13 51:3 - 53:6, 55:22 - 57:4; Vailhe 6/20/13 182:2 185:5.

[42] Heniford Video, *supra*, n. 36.
[43] Id.
[44] Eth.Mesh.05920616 7/20/07 Email from Chomiak, Marty Subject: Defining Light Weight Mesh.
[45] Batke 08/01/13 87:12 - 88:10, 113:3 - 114:3, 257:23 - 259:13; Holste 07/29/13 51:3 - 53:6, 55:22 - 57:4; Vailhe 6/20/13 182:2 - 185:5.

mesh and continues to promote and sell the product with the same, heavy weight, thick filament "Old Construction 6 mil" mesh that they have been selling since 1974 (Prolene), despite what Ethicon considers to be "revolutionary" advancements in polypropylene mesh design that it brought to other pelvic floor polypropylene mesh products.[46] I have reviewed the expert report of Dr. Uwe Klinge, in which he performed histopathological analysis on the same 23 explant samples of TVT and TVT-O that Dr. Jordi performed degradation testing. Dr. Klinge found that all of the pathology slides from these explants showed extensive fibrotic bridging and 19/21 showed folding or shrinkage.

In summary, for the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT causes fibrotic bridging in the body, resulting in an increased inflammatory response leading to a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

[46] Eth.Mesh. 03905968

5. *Mesh Contracture/Shrinkage*

Mesh contracture or shrinkage is an event that takes place after the implantation of mesh and relates to the wound healing process that occurs after the surgical trauma of implanting a foreign body made of polypropylene in the sensitive tissues of the vagina and the pelvis. By 1998, polypropylene mesh was known to contract or shrink 30-50%.[47] Contraction or shrinkage has been shown to draw nerves close to the midurethral sling mesh both in the transobturator application[48] and for retropubic application.[49]. Furthermore, contraction or shrinkage is closely related to the pore size of the mesh. Small pores lead to fibrotic bridging leading to scar plates, mesh encapsulation and shrinkage or contraction of the mesh, which is a compound and combines with the effect of the normal wound healing process that is already occurring in the tissue

This phenomenon of shrinkage and its relation to the design of the pores as well as the consequences to the patient were illustrated in an email by Ethicon Scientist Joerge Holste in a March 13, 2006 email discussing a paper he authored entitled "Shrinking Meshes?"[50] In his email, Dr. Holste states "this was our scientific statement on mesh shrinkage: Basically, small pores, heavy weight meshes induce more fibrotic bridging tissue reaction causing more mesh shrinkage during maturation of the collagenous tissue. See my presentation about biocompatibility."[51] In addition, in a presentation by Boris Batke, Associate Director R&D, he

[47] Klinge, U, "Shrinking of Polypropelen Mesh in Vivo: An Experimental Study in Dogs," Eur J Surg, 1998 (164:965-969); Jacquetin, B, "Complications of Vaginal Mesh: Our Experience," Intl Urogyn J, 2009 (20:893-6); Tunn, R, "Sonomorphological Evaluation of Polypropylene Mesh Implants After Vaginal Mesh Repair in Women with Cystocele or Rectocele," Ultrasound Obstetrics Gynecol, 2007 (29:449-452).
[48] Corona, R, et al., "Tension-free Vaginal Tapes and Pelvic Nerve Neuropathy," J Min Invas.Gynecol, 2008 (15:3 262-267); Parnell, BA, et al.,"Genitofemoral and Perineal Neuralgia after Transobturator Midurethral Sling," Obstet Gynecol, 2012 (119:428-431).
[49] (Heise CP, et al., "Mesh Inguinodynia: A New Clinical Syndrome After Inguinal Herniorrhaphy?" J Am Coll Surg 1998 (187:5 514-8); Voeller, GR, Surg. Technol. Intl. 2003.
[50] Eth.Mesh 05446127, *supra*, n. 34.
[51] Id.

states heavier-weight polypropylene mesh results in mesh contraction of 33%.[52] Ethicon was aware that the mesh in TVT would shrink as well. Specifically, in an email dated November of 2002, related to a discussion of mesh used in a TVT product, it states that Axel Arnaud, one of Ethicon's medical directors, used 30% shrinkage of the mesh as a "rule of thumb."[53]

At an Ethicon expert meeting in Norderstedt, Germany in 2007, an Ethicon employee presented a PowerPoint entitled "Factors Related to Mesh Shrinkage" in which all of these issues were clearly laid out.[54]

Mesh shrinkage was known by Ethicon as early as 1998 in published work by Ethicon's then consultants, Uwe Klinge and Bernd Klosterhalfen.[55] They noted in these early papers that all polypropylene meshes shrink 30-50%. This was restated in later works by W Cobb and his colleagues[56]– one of which was Dr. Henniford (referenced above). The works of Cobb and Klinge/Klosterhalfen have been referenced in numerous Ethicon documents and thus, Ethicon was well aware of these findings regarding the shrinkage or contraction of polypropylene meshes in vivo. Ethicon was further aware that heavier weight meshes led to greater amounts of contraction.[57]

It is my opinion to a reasonable degree of medical certainty that as a result of work with internal and external experts and consultants in the late 1990s, multiple internal documents and articles, and the scientific literature as a whole, Ethicon was or should have been aware that

[52] Eth.Mesh 05479717 3/1/11 Boris Batke, Ethicon Associate Director R&D, Presentation: Ethicon Polypropylene Mesh Technology.
[53] Eth.Mesh 03917375
[54] Eth.Mesh. 02017152, Nordestadt Expert's meeting 2007, Eth.Mesh.01782867, "Factors Related to Mesh Shrinking."
[55] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969

[56] Cobb W, Kercher K, Heniford T. The Argument for Lightweight Polyropylene Mesh in Hernia Repair. Surgical Innovation. 2005; 12(1):T1-T7
[57] Id.

shrinkage of its Prolene mesh not only could, but would, occur and that this shrinkage could lead to painful complications in women implanted with TVT, such as multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

6. *Particle Loss, Fraying, Roping and Curling, Loss of Pore Size*

Since the development of TVT, Ethicon has been aware that Prolene tape frays upon stretching.[58] As early as 2000, Ethicon was aware that particles from TVT Prolene mesh fell into the tissue as a result of the tape edges being damaged during sheath removal.[59] In April 2001, Dr. Alex Wang, "one of the most experienced TVT users in the world," reported problems with frayed mesh and uneven tape width.[60] Although the issue was described as "serious" and as requiring "urgent attention and solution," Ethicon Medical Director, Dr. Martin Weisberg, simply concluded that the deformity in the mesh would be *unlikely* to have any clinical significance. Dr. Weisberg testified that although he did not actually know whether frayed mesh

[58] Weisberg 5/31/00 461:7-462:3.
[59] Eth.Mesh.01317515 7/12/00 Preventia TVT-2 Risk Analysis Procedure/Tensioning Frayed Mesh/Particle Loss at Eth.Mesh.01317523.
[60] Eth.Mesh.03905472 6/4/01 Emails from Wang, Dr. Alex Subject TVT Recommendation for Ethicon Study of Fraying/Particle Loss.

leading to particle loss would have clinical implications, he does not recall whether he or anyone else at Ethicon studied the issue.[61] Just a few months later, however, Ethicon received a complaint by an experienced surgeon regarding a patient who experienced vaginal wall erosion following a TVT procedure which was first noted by her husband during intercourse. According to the surgeon, "the tape appeared frayed and tiny fibers were protruding through the vaginal wall."[62]

In November 2003, Dr. Weisberg reported that there had been a total of 58 complaints of fraying with TVT since introduction of the device in 2000. He observed that the following occurs when the mesh frays: "[T]he mesh elongates in places; the mesh narrows in places; and small particles of Prolene might break off … and that [s]tretching of the mesh increases the probability of fraying."[63] Once again, however, Dr. Weisberg concluded that "since fraying does not affect the safety and efficacy of the TVT device, it has been determined not to pursue any corrective actions at this time."[64] Dr. Weisberg confirmed during his deposition that no corrective action was taken and, although he did not know whether Prolene particles could elicit a chronic foreign body response, he does not recall whether he or anyone else at Ethicon investigated the issue.[65]

In 2004, Ethicon continued to receive complaints from surgeons about fraying and "brittle" mesh and particles falling into the operating field.[66] One of the company's "most urgent customers," Swiss surgeon Dr. J. Eberhard, wrote the following: "Already at the operation it is

[61] Weisberg 5/31/13 469:23-470:16.
[62] Eth.Mesh.02621559 at Eth.Mesh.02622276 Ethicon Issue Report TVT Retropubic 2001 Open Date Between 01-Jan-2001 and 31-Dec-2001.
[63] Eth.Mesh.00541379 11/18/03 Memo from Weisberg, Dr. Martin Subject: Mesh Fraying for TVT Devices Inadequate Testing.
[64] Ibid.
[65] Weisberg 5/31/13 469:23-470:16.
[66] Eth.Mesh.00863391 at Eth.Mesh.00863392 2/27/04 Emails from Smith, Dan Subject 2 TVT Complaints Concerning Allegedly Brittle Mesh.

embarrassing to see how the tape is crumbling. But it gets worse if there is stretch on the tape. … I can't understand, that no one will solve that problem for such a long time. As the latest, as the tape has becoming blue, everyone has realized, that the quality of the tape is terrible."[67]

Once again, however, Ethicon decided to take no corrective action.[68] Instead, sales representatives were instructed to reassure their doctors that, "Prolene is proven to be inert," the "particles will not cause any problem," and to "be proactive" because "the competition will try to target this!"[69] Physicians were told the particles are "non-reactive" and that fraying does not affect the safety or efficacy of the device.[70]

In fact, it has consistently been Ethicon's position that frayed mesh and resulting particle loss as well as roping, curling and deformation of the mesh do not create a safety risk and have no clinical significance. [71] On the contrary, Dr. Pariente published a study that concluded that "the very high particle shedding for both Sparc (AMS) and TVT (Ethicon) may be of significant long term clinical concern in some quarters."[72] Although Ethicon claims that its own internal testing shows approximately 1% particle loss with TVT,[73] Dr. Pariente's study demonstrated TVT particle loss as high as 8.5% - 10 times higher than most of its competitors.[74]

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[67] Eth.Mesh.02180833 11/12/04 Letter from Prof. Dr. Eberhard (translated); Eth.Mesh.02180828 11/12/04 Telefax from Sibyll, Basso to Menneret, David re Prof. Dr. Eberhard.
[68] Eth.Mesh.02180826 11/12/04 Email from Menneret, David to Smith, Dan and others Subject Mesh Fraying: Dr. Eberhard Letter.
[69] Eth.Mesh.00865322 3/2/04 Email from Bell, Steve, Ethicon Marketing Director Europe to Sales & Marketing Team Subject: Reminder on Blue Mesh – Frayed Mesh/Particle Loss.
[70] Eth.Mesh.03535750 10/12/2005, Hunsicker, MSN, CRNP, Kimberly, Ethicon Clinical Operations Regional Manager, Presentation: Investigator Initiated Study Process – Inadequate Testing.
[71] Eth.Mesh.00541379, *supra*, n. 58; Eth.Mesh.00858252 2004 Memo from London Brown, Allison, =to Smith, Dan Subject Mechanical Cut v. Laser Cut Mesh Rationale.
[72] Eth.Mesh.01221055 Pariente, J-L, "An independent biomechanical evaluation of commercially available suburetheral slings," Issues in Women's Health,2003.
[73] Eth.Mesh.000585802, or 6/12/06 Kammerer 00585842; Eth.Mesh.00585823 06/27/06 Email from Kammerer, Gene to Volpe, Clifford, Subject GY: ***URHENT*** French STANDARD ON TVT & MESHES (COMMENTS REQUIRED)
[74] Eth.Mesh.01221055, *supra*, n. 67; Eth.Mesh.00585842 6/12/06 Email from Kammerer, Gene to Rha, Sunny Subject TVT LCM – Particle Loss (Reimbursement Submission); Eth.Mesh.01219629 5/09/06 Email from Flatow, Jacqueline to Kammerer, Gene Subject: Re: Particle loss on TVT; Eth.Mesh.01221024 Email 5/04/06 from

Ethicon also knew very early on that the TVT mesh would rope, curl and become deformed when under tension. Again, Ethicon claimed that these problems with the mesh did not have any clinical significance despite the fact that surgeons were complaining.[75] This is not true according to Ethicon's own internal documents, including its risk analysis related to the TVT mesh. [76] The loss of pore size due to mesh narrowing or deformation may also lead to urinary retention or erosion. Ethicon's own dFMEA shows that Ethicon recognized in 2006 that the hazards of curling/roping, frayed edges and inadequate pore size of mesh can lead to the harms of erosion, recurrence, and pain.[77]

When discussing the dFMEA for Laser Cut Mesh, Former Medical Director, David Robinson, agreed that pore size of both the Laser Cut and Mechanically Cut mesh "[c]ould reduce, the tissue might not encapsultate . . . the tissue might not grow through the mesh. It can become encapsulated and then it could cause . . . a rejection of the mesh."[78]And, Dr. Robinson believes a rejection of the mesh can lead to an erosion.[79]

Ethicon has had reports of TVT mesh curling, narrowing, or deforming under tension. These changes in the mesh may lead to erosion or pain for women with the deformed mesh implanted in their bodies. Further, according to Ethicon, this curling, roping or narrowing of the mesh may also cause urinary retention in addition to erosion and pain. [80]

Kammerer, Gene to Fourneir, Herve and Arnaud, Axel Subject: New Standards for Urethral Slings; Eth.Mesh.00585823, *ibid*.

[75] Eth.Mesh 00440005; Eth.Mesh 00302390 TVT-Base & TVT-O Review for Laser Cut Mesh (LCM) Risk Analysis

[76] Eth.Mesh.01218019.

[77] Eth.Mesh.01218019.

[78] Robinson 9/11/13 1070:23-1072:25.

[79] Ibid.

[80]Robinson, 9/11/13, 1079:3-4-1081; 1081:9-13;1083:8-18; Eth.Mesh.01218019, Eth.Mesh 01822361.

Engineers at Ethicon knew that TVT could cause more urinary retention than some of its other meshes because the mesh will "curl and rope which reduces the surface area of the mesh under the urethra and therefore, increases the pressure in a localized point". [81] In fact, I have witnessed the same type of roping and narrowing of TVT when I placed them myself and can see the deformed and roped mesh when I remove them. This localized pressure under the urethra leads to complications like, among others, urinary retention, chronic pain, dyspareunia and erosions. In addition, I have reviewed Ethicon TVT training videos that show the exact problem discussed about related to deformation and roping of the "tape" under the urethra. [82] Finally, according to Ethicon's Dan Lamont, it chose to continue to sell "mechanically cut mesh despite knowing that it had the potential for degradation, particles floating around in women's bodies, stretching, and roping . . ."[83] Lamont admitted that the fraying of the mesh was a "defect" of the mesh. [84]

In 2005, Ethicon developed laser cut mesh presumably in an effort to address the chronic problems with particle loss, fraying and elongation seen with mechanically cut mesh.[85] Astonishingly, as part of the design verification activities, Ethicon initially decided that particle loss, elongation curve and flexural rigidity data would *not* be required because they were not

[81] Eth.Mesh.01822361 Email from Dan Smith re TVT Secur.
[82] Eth.Mesh.PM.000004 TVT Retropubic Implantation Video.
[83] Lamont 9/11/13 30:18-24
[84] Lamont 9-11-13, 15:16-16:10

[85] Eth.Mesh.00301741 11/21/05 Emails from Lamont, Dan Subject: !!!!GREAT NEWS FOR TVT LASER CUT MESH!!!! –Frayed mesh/particle loss; Eth.Mesh.00394544 2/01/06 Global Regulatory Strategy – GYNECARE TVT – Laser Cutting Project; Weisberg 5/31/13 487:13-488:7.

"critical to quality."[86] In fact, this news was celebrated as "!!!!!GREAT NEWS FOR TVT LASER CUT MESH!!!!" and "less work for all of us."[87]

Because the reason for developing laser cut mesh was to eliminate particle loss, Ethicon ultimately decided that some minimum testing comparing particle loss of mechanical cut mesh verses laser cut mesh would be required.[88] Test results showed that while the average particle loss for mechanical cut mesh was higher, the difference in particle loss between mechanical cut mesh and laser cut mesh was *not* statistically significant.[89] Furthermore, laser cut mesh has since been found to have differing mechanical properties. For example, Professor Carl G. Nilsson, who has been described by Ethicon as a "founding father" of TVT,[90] "will not use Laser-cut mesh!!" as it "does not have the same stretch profile of Mechanical-cut mesh."[91] Finally, in 2006, an Ethicon Engineer, Gene Kammerer, made a presentation that showed photos of TVT mesh being stretched. These photos clearly show particle loss, fraying, degradation, roping and deformation when the TVT mechanical cut mesh was stretched and compared to TVT Laser Cut. [92] In fact, as discussed above, according to Dan Lamont, Ethicon chose to continue to sell its "mechanically cut mesh despite knowing that it had the potential for degradation, particles floating around in women's bodies, stretching, and roping . . ."[93]

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[86] Eth.MeshIbid; Weisberg 5/31/13 490:15-491:17.
[87] Eth.MeshI ibid.
[88] Ibid.; Eth.Mesh.00584291 2/15/06 Email from Flatow, Jacqueline to Rha, Sungyoon, Kammerer, Gene and Lamont, Dan Subject RE: DVer protocol for particle loss.
[89] Eth.Mesh.01219984 3/20/06 CPC-2006-0014, Completion Report for the Design Verification of TVT Laser Cut Mesh Particle Loss at 50%Elongation; Eth.Mesh.00585842, *supra*, n. 68.
[90] Eth.Mesh.00858891 2/29/08 MiniMe R & O Final.
[91] Eth.Mesh.04048515 at Eth.Mesh.0408516 7/01/08 KOL Interview: Carl G. Nilsson, Project Scion.

[92] Eth.Mesh 03334244; Eth.Mesh 06001408; Eth.Mesh 00584527
[93] Dan Lamont, 9/11/13, 30:18-24

In addition, Ethicon's April 2006 Clinical Expert Report on TVT Laser Cut Mesh suggested there was a decrease in particle loss with laser cut mesh and this "decrease would lead to less non-functioning material left in the tissues."[94] Interestingly, the greater the nonfunctioning material left in the patient's tissue, the greater the surface area of polypropylene the patient is exposed to, and the greater the inflammatory responses and the greater the foreign body response. As discussed above, the long term consequences of this chronic foreign body reaction and inflammatory response can be, among other things, chronic pain, lifelong risk of erosions, dyspareunia and failure of the device. If the individual flakes work their way through the vaginal mucosa, this can lead to dyspareunia and/or painful intercourse for the partner as noted in the complaint received by Ethicon back in 2001 referenced above. The larger the surface area the greater the risk associated with vaginal mesh. Finally, detached flakes of polypropylene may migrate into the vasculature or lymphatics and cause problems remote from the pelvis.

In summary, for the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT has several characteristics that make it improper for use in the vaginal canal including particle loss, fraying, roping, curling, deformation and loss of pore size. These unwanted characteristics can lead to, among other things, an increased inflammatory response (particle loss and fraying) and/or increased pressure on the urethra (roping or curling) or loss of pore size (roping or curling), and can lead to a multitude of injuries, including such as multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and

[94] Eth.Mesh.00167104- at Eth.Mesh.001617109.

defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its Prolene mesh in a permanent prosthetic implant like TVT.

B. Ethicon's Disclosures of Adverse Events in its TVT IFU Have Been Inadequate Based on the Adverse Reactions/Risks Known to Ethicon from the time the TVT was first sold and marketed.

The purpose of the IFU is for a medical device manufacturer to provide physicians with the information necessary for them to make decisions regarding the medical device for a particular patient. In addition, the IFU should disclose adverse reactions and risks known to the medical device manufacturer to the physician so that the risks can be relayed to the patient and an informed decision regarding the use of the product can be reached. Throughout my education, training, surgical and clinical practice, I have reviewed numerous IFUs for a variety of products, including mesh products in order to understand the proper way to use the device and to gain knowledge about the complications and adverse events associated with a device. I have extensive clinical experience with IFUs and instructing patients about the adverse events/risks contained in the IFU. Similar to Medical Directors, Dr. Martin Weisberg and Dr. David Robinson, I have gained expertise in IFUs through me extensive clinical experience reviewing IFUs, consenting patients regarding IFUs, including Ethicon's own pelvic mesh products including the TVT line and Prolift.

As seen in the deposition of Catherine Beath, Ethicon's former Vice President of Quality Assurance and Regulatory Affairs, "physicians should be made aware of all the significant safety

risks associated with the product in the IFU."[95] And, "a reasonably prudent medical device company would continually update the label consistent with developing data and information that becomes known to the company" when it is appropriate.[96] It is also true that the medical affairs department has the final say over regulatory affairs as to what warnings need to be given.[97] In fact, according to Ms. Beath, regulatory affairs defers to medical affairs as to what warnings need to be given.[98] And, medical affairs has authority to ask for label changes.[99]

Similarly, former Medical Director Dr. David Robinson testified that the warnings and adverse event section of the IFU should include all significant risks and complications related to the procedure and the mesh. [100] According to Dr. Robinson, a device manufacturer must include this information because you want to make sure the doctors have all the information they need to adequately inform patients who are deciding to use the product. [101]

According to Ethicon Medical Director Dr. Martin Weisberg, the goal of the IFU is to communicate the most important safety risks attributable to the TVT device and that an IFU should never exclude known hazards or complications.[102] Dr. Weisberg also believes that an IFU should not knowingly underestimate the risks of using the product.[103] And, if an IFU excludes known complications or understates the risks, it "fails in one of its principal purposes." [104]

From the time the TVT was first sold for present day, there are six versions of the Ethicon TVT IFU. These include the following versions: September 8, 2000, December 22,

[95] Beath 7/12/13 592:7-11.
[96] Beath, 7/11/13, 198: 8-13
[97] Beath, 7/12/13,610:12-15
[98] Id., 7/l2/13, 610:12-15

[99] Id., 7/12/13, 610:21-611:1
[100] Robinson\, 9/11/13 238:12-25.
[101] Robinoson 9/11/13 239:1-11.
[102] Weisberg 8/9/13,659:19-660:15
[103] Id at 960:13-16.
[104] Id at 961:10-17.

2003, February 11, 2005, April 7, 2006, October 13, 2008 and November 29, 2010. A chart showing the Adverse Reactions/Risks section for each version of the TVT Instructions for Use is set forth below.

Product	Production Prefix	Start Bates	End Bates	First Use Date	Last Use Date	Adverse Reactions / Risks
TVT	ETH.MESH.	5225354	5225385	09/08/00	11/26/03	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	2340306	2340369	12/22/03	02/11/05	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	2340471	2340503	02/11/05	04/07/06	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize

						the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	5222673	5222704	*4/07/06*	10/07/08	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	2340504	2340567	10/13/08	11/22/10	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	3427878	3427945	11/29/10	To Present Day	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination.

						* Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.

In all six versions of the TVT IFU from the launch of the product to present day, the Adverse Reactions/Risks section has remained exactly the same (ASK ANDY TO CONFIRM) . It reads as follows:

ADVERSE REACTIONS

* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair.

* Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation.

* As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination.

* Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.

Despite only listing the above adverse reactions/risks, it is clear from the testimony of Senior Ethicon Employees in both the Medical Affairs and Regulatory Affairs that every adverse reaction/risk that Ethicon is aware of today, it knew about at the time the TVT was first sold,

marketed and launched.[105] Medical Director, Piet Hinoul testified that Ethicon was aware of the following adverse events from the time the TVT was first sold [106]:

Erosions through vaginal epithelium
Infection
Pain
Urinary Problems
Erosions that could decrease patient's quality of life
Dyspareunia
Need for additional surgeries
Need for the removal of device
Urinary Tract Infections
Dysuria
DeNovo Urgency
Mesh Exposure
Fistual Formation
Hematoma
Abscess Formation
Narrowing of vaginal wall
Erosion which can occur any time in future
Contracture of mesh causing pain
Complications making it impossible to have sexual relations
Worsening Incontinence

Additionally, Catherine Beath, VP of Quality of Assurances and Regulatory Affairs when discussing the October 20, 2008 FDA Public Health Notification (PHN)[107] testified that Ethicon was aware of all of the risks outlined in the PHN at the time of the launch of the TVT line of products. In other words, Ethicon had knowledge of all of the risks listed in the 2008 PHN at the time it launched the TVT. [108]

Interestingly, in 2008, 2011 and 2012, Ethicon added numerous adverse reactions and risks to its Patient Brochures have never been disclosed in previous versions of the Patient

[105] Beath, 7/12/13,608:13-20; Hinoul, 6/27/13, 551:12-552:9; Arnaud, 7/19/13,114:21-127:1

[106] Hinoul 7/27/ 13 542:11-582:13.
[107] Eth.Mesh 07937826 2008 FDA Health Notification.

[108] Beath 7/11/13 233:25-234:8, 245:21-246:1.

Brochures. These adverse reactions and risk have never been disclosed in the TVT IFUs even at present time. These risks are as follows:

From Patient Brochures (never in IFU)

2008
Difficulty urinating
Pain
Scarring
Mesh Exposure requiring treatment

2011

Mesh exposure into the vaginal canal
Mesh exposure associated with pain during intercourse for the patient and partner[109]
Mesh exposure which may require removal of exposed mesh in the office or operating room

2012

Pelvic Pain
Development of Urinary Incontinence
Voiding Difficulties
Hemorrhage or hematoma
Urinary tract infection
Wound healing problems
Injury to ureters
Pelvic abscess formation
Risk of infection
Vaginal scarring
Mesh contracture (mesh shortening due to scar tissue)

[109] It should be noted that this adverse reaction/risk was taken out of the 2012 Patient Brochure.

For a surgeon to properly inform the patient of all the known risks involved in any procedure involving an implantable medical device, the surgeon relies upon the manufacturer to be aware of and convey all characteristics of its products that could impact safety and efficacy. Specifically, surgeons rely on the "Adverse Events/Risks" section of a medical device IFU to gain knowledge regarding adverse events or undesirable effects that the company knows are associated with the product.

If you compare the adverse reactions/risks in the TVT IFUs to the adverse reactions/risks Ethicon knew at the time of the launch of TVT, it is clear that there are numerous adverse events absent from the IFU. Again, Ethicon and its VP of Quality Assurance and Regulatory Affairs, Catherine Beath, believe that all "physicians should be made aware of all the significant safety risks associated with the product in the IFU."[110] Ethicon's Medical Director, Dr. Weisberg, believes the goal of the IFU is to communicate the most important safety risks attributable to the TVT device and that an IFU should never exclude known hazards or complications.[111]

Even though Ethicon changed its Patient Brochures in 2011 and 2012 to include additional significant adverse events/risks, it never added the same information to the TVT IFU. This is true despite the fact that Ethicon had internal discussions about updating the IFU in 2009 after the 2008 FDA Public Health Notification (PHN). Specifically, a meeting was held to and one of the purposes of the meeting was to decide if "the current Adverse Reaction of tape exposure and post-operative dyspareunia in the TVT-family products . . .[112]

After discussing the 2008 PHN, competitors labels and Remetrex issues, impressions were that tape exposure/erosion/extrusion very frequently reported, patients did not feel there

[110] Beath, 7/1213 592:7-11.
[111] Weisberg 8/19/13, 659:19-660:15.
[112] Eth.Mesh 04081189

were adequate pre-op consent or risk-benefit assessment, patient specific concerns about exposure/erosion/extrusion, incontinence recurrence, post-operative dyspareunia and pain-affect quality of live and affect daily routine, re-operations and post-operative complications disproportionate to pre-operative-consent-expectations. [113]

Despite these discussions and Ethicon's knowledge of these serious, devastating and life-changing adverse events/risks, to this day, it has never updated or changed its IFU to include this information.

Ethicon failed to include significant adverse events and risks in its IFU for TVT, including, permanent, lifelong and debilitating pelvic pain, lifelong sexual complications and dysfunction, urinary problems, worsening incontinence, lifelong risk of multiple surgeries, need for removal of the device, lifelong risk of erosions, and the risk of serious complications and effect on a patient's quality of life. In addition, as discussed more fully above, Ethicon failed to include significant risks in its IFU related to the Prolene polypropylene mesh, including potential cytotoxicity, association with tumor formations and that the mesh can degrade, shrink and contract. The IFU also fails to include risks associated with the Prolene mesh, including chronic foreign body reaction, fibrotic bridging, infections/biofilms, fraying/particle loss and roping/curling of the mesh.

In fact, Medical Director Dr. Weisberg testified that Ethicon did not include: "permanent, lifelong, worsening and debilitating pain", lifelong risk of surgical repairs for erosions, "severe or chronic inflammation, "collapse under strain and cause fibrotic bridging, that the product can degrade, that polypropylene is cytotoxic, severe erosion, or particle loss. [114]

[113] Eth.Mesh 04081189
[114] Weisberg, /19/13, 968:12-972:21.

In addition, former Medical Director, Dr. David Robinson, recently testified that Ethicon never informed physicians that patients may require multiple surgeries to treat erosions, that erosions could be severe and untreatable, that patients could endure lifelong severe pain or dyspareunia/painful sex. This is true despite, as discussed above, Ethicon knew of the risks at the time of launch. In summary, Physicians were not fully informed about numerous adverse reactions/risks associated with the TVT despite the fact that Ethicon had knowledge of the risks from the time the product was first sold. As a result, physicians were unable to fully consent and inform patients of the risk associated with TVT. To a reasonable degree of medical certainty, Ethicon fell below the standard of care required of a reasonable medical device manufacture by failing to adequately disclose these known risks to physicians. This prevented physicians and patients the ability to make an informed choice regarding the use of the TVT.

In addition, to this day, Ethicon significantly downplays the risks that it actually lists in its IFU. This is especially true with respect to erosions. On the topic of erosions, in the Adverse Event/Risks section in the TVT IFU, in place from the time of launch until present day, it states:

> * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation.

This language significantly downplays the permanent nature of erosions and suggests to physicians that erosions are a "transitory" or temporary problem. This is best portrayed by an email exchange between Ethicon's Associate Medical Director of Worldwide Customer Quality Meng Cheng, M.D., Ph.D and Bryan Lisa in the Regulatory Affairs Department in a January 29, 2009.[115] When discussing the transitory language and possible insufficiencies regarding that

[115] Eth.Mesh.04093125 1/29/2009 Email between Meng Chen and Bryan Lisa.

language in the IFU, Dr. Cheng tells Bryan Lisa in Regulatory Affairs "Pardon me again, from what I see each day, these patient experiences are not "transitory" at all."[116]

Ethicon also knew that erosions could occur many years after implantation of the device. In Minutes from June 22, 2001 Scientific Advisory Committee on Pelvic Floor Repair, it was a "Consensus: Erosion is a risk. Erosion, possibly an infection response. Typically seen by 3 mos, usually by 6-12 mos. Can present late, 3 years. To vagina-not a good situation. To bladder, urethra or rectum-a very bad situation."[117]

In October 2002, Medical Director Dr. Martin Weisberg was involved in email exchange with European Science Director Axel Arnaud about downplaying risks with respect to erosions. Specifically, Dr. Arnaud suggested to Dr. Weisberg that Ethicon needed "to be more elusive" when discussing potential complications like erosions.[118]

According to Medical Director Dr. Martin Weisberg and former Medical Director Dr. David Robinson, Ethicon never disclosed or warned doctors or patients in IFUs or Patient Brochures that the use of TVT slings can cause lifelong risk of erosions.[119] Rather, Ethicon downplayed the risks of erosions by implying that they are transitory. Despite the fact Ethicon had knowledge from one of its own doctors that experiences were not transitory and that she had concerns about the IFU and the transitory language, Ethicon never informed physicians or disclosed it in its IFU.

As discussed above, despite the scientific literature, its own internal dog study and reports from consultants it hired that state degradation of the mesh occurs, Ethicon's IFU states that the mesh in the TVT "is not absorbed, nor is it subject to degradation or weakening by the

[116] Id.
[117] Eth.Mesh.02089392.
[118] Eth.Mesh.03910175-03910177.
[119] Weisberg 8/19/13 968:2-969:10; Robinson 9/11/13 329:12-330:7.

action of enzymes." [120] This is simply inaccurate for all of the reasons above, including, most importantly, Ethicon's own internal documents and testimony from its employees. Specifically, Ethicon's only study (7 year dog study) related to degradation and its Prolene material shows that it does in fact degrade over time.[121] Dan Burkley, Senior Scientist in Research and Development, confirmed that the 7 year dog study and photos showed that the mesh in the TVT degraded.[122]

Ethicon not only failed to disclose risks, but also downplayed significant risks by calling them transitory and by putting inaccurate statements about degradation in its IFU. This is information physicians need to know in order to have a fair and proper conversation with their patients about the use of a product. Physicians rely on device manufacturers to inform them of the risks and complications associated with its products instead of downplaying them or inaccurately stating them. By not disclosing this safety information to physicians and their patients, to reasonable degree of medical certainty, Ethicon failed to act like a reasonable and prudent device manufacturer in this regard.

C. Ethicon did not disclose to physicians in its IFUs information regarding characteristics of Ethicon's TVT mesh (Prolene) that make it unsuitable for its intended application as a permanent prosthetic implant for stress urinary incontinence, including that it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, and fraying, particle loss, roping and curling, and loss of pore size.

As discussed above in section IV, B, the goal of the IFU is to communicate the most important safety risks attributable to the TVT device and that an IFU should never exclude known hazards or complications.[123] In addition, according to Ethicon's Medical Director, an

[120] Eth.Mesh.05225354, Eth.Mesh.02340306, Eth.Mesh.02340471, Eth.Mesh.05222673, Eth.Mesh.02340504, Eth.Mesh.03427878.
[121] Eth.Mesh.05453719.
[122] Burkley 5/23/12 315:8-13.
[123] Weisberg, 8/19/13, 659:19-960:15.

IFU should not knowingly underestimate the risks of using the product.[124] And, if an IFU excludes known complications or understates the risks, it "fails in one of its principal purposes."[125] Again, this is true because it is imperative for physicians to know about hazards and harms related to a product so that they can have an accurate conversation with their patient about the use of the product. If a physician does not have important safety information, he/she cannot pass that information to their patient so that an informed decision can be made about the use of the product.

As discussed above in section IV. A., Ethicon knew about significant harms and hazards related to the Prolene mesh used in the TVT. These harms and hazards include that the mesh degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, and fraying, particle loss, roping and curling, and loss of pore size. However, despite its knowledge regarding these harms/hazards as discussed in detail in section IV., A. above, Ethicon never disclosed this information to physicians in its IFU. As a result, physicians are not able to have a fully informed conversation with their patients about the safety of the TVT device. By inadequately disclosing this information, Ethicon failed to act in as a reasonable and prudent medical device manufacturer.

D. Ethicon failed to adequately describe, inform or explain to physicians how to properly "tension" the TVT and inform them that improper tension on the mesh decreased effective pore size and interfered with incorporation into tissue.

TVT stands for and has consistently been marketed by Ethicon as "Tension-free Vaginal Tape."[126] Presumably, this means the mesh should be inserted under the urethra without tension. However, the term "tension-free" is misleading. In practice, too little or no tension

[124] Id at 960:13-16.
[125] Id at 961:10-17.
[126] Smith 6/4-5/13, 610:18-611:11; 1186:9-16.

results in failure to treat the underlying condition of urinary incontinence. On the other hand, as suggested by Ethicon's own internal documents, too much tension can result in serious complications such as urethral erosion.[127]

The IFU provides little guidance on proper tensioning of the TVT. Specifically, once the tape is placed, surgeons are simply instructed to pull the needles upwards "to bring the tape (sling) loosely, i.e. without tension, under the midurethra" and to "adjust the tape so that leakage is limited to no more than one or two drops." [128] The IFU's Warnings and Precautions section cautions surgeons to "[e]nsure that the tape is placed with minimal tension under the mid-urethra." [129] Yet in the very same section, the surgeon is instructed "to place the tape tension-free in the mid-urethral position" to minimize the risk of de novo detrusor instability.[130] Finally, the IFU's "Adverse Reactions" section provides that "over correcting, i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction." [131] The IFU's conflicting instructions with regard to tensioning of the tape, i.e. "without tension," "with minimal tension," "tension-free" and "overcorrecting, i.e. too much tension" are clearly confusing and inadequate despite the fact that Ethicon knew as early as 2000 that improper tensioning could lead to complications and, therefore, the IFU needed to be "clear." [132]

Ethicon recognized as far back as November 1999 that TVT tension adjustment was considered "high need" and surgeons had a hard time sticking to proposed technique.[133] By 2000, Ethicon recognized that excess tensioning during initial placement could create a risk of

[127] Eth.Mesh.05529274; Eth.Mesh.04044797; Eth.Mesh.05529653; Eth.Mesh.00161131.
[128] Eth.Mesh.05222686, emphasis added.
[129] Eth.Mesh.05222687, emphasis added .
[130] Eth.Mesh.05222567, emphasis added.
[131] Eth.Mesh.05222687, emphasis added .
[132] Eth.Mesh.01317523 .
[133] Eth.Mesh.05641096 .

erosion.[134] In an email dated February 13, 2001, Medical Director Axel Arnaud wrote "there is clearly a need for standardization of the TVT procedure to avoid excessive tension on the mesh. We should aggressively work in order to develop a product and I would like to take the responsibility for this." [135] In May 2002, Axel Arnaud continued to recognize the need to develop a safer device "in order to prevent excess tension of the tape."[136] In 2003, Ethicon recognized that a challenge with the TVT procedure remained complications "associated with over-tensioning of the sling and the inability to obtain precise biofeedback and adjustment during and/or after the procedure."[137]

The lack of clear direction on tensioning in the IFU is demonstrated in September 2004 emails from Sales Representative Shannon Campbell in which she writes: "What is a huge challenge to a rep trying to make this right, is that we really don't know what the right amount [of tensioning] is. We know this is a quick fix to the problem, but not a clinically backed solution. It's almost like trying to decide if a 8, 10, or 12 mm hagar dialator is best for tensioning TVT with the patient under general. We learned the cough test, but relied on surgeons experience with the tensioning under general…. This has been such a gray area and everyone seems to have their own tensioning technique." She continues: "I feel I got a little grilled over my suggestion of tensioning, yet there is no clear direction on tensioning. I'm not a rebel looking for my own way of doing this. I'm a rep trying to figure out what is best from my experience with surgeons and what I see the product doing in the OR. …The reason for my question is to see if someone

[134] Eth.Mesh.05529274; Eth.Mesh.04044797; Eth.Mesh.05529653; Eth.Mesh.00161131.
[135] Eth.Mesh.03915380.
[136] Eth.Mesh.03907468.
[137] Eth.Mesh.00259271.

had the proper wording we need to use as rep's that eliminates our liability with the product in the OR concerning tensioning."[138]

In December 2006, Ethicon Marketing Director Allison London-Brown referred to tensioning as a "sticky" question and acknowledged that "we cannot accurately describe [tensioning] in writing." Meanwhile, Ethicon knew that patients were suffering from erosions and, in fact, would often blame the physician as the cause of the erosion for putting "too much tension on the device." [139]At least by 2007, it seems Ethicon finally acknowledged that "TVT has never been tension free!" despite years of marketing it otherwise.[140] For example, in 1999, Ethicon utilized marketing pieces for "TVT Tension Free Vaginal Tape" which claimed "Tension-free Support Only When Needed" which "reduces possibility of urethral erosion." [141] A 2001 marketing piece for "Gynecare TVT Tension-Free Support for Incontinence" claimed "most complications are minor and are avoidable with adherence to procedural technique and instructions for use."[142] In 2004, during the same time period when Shannon Campbell was lamenting the problems with tensioning, Ethicon continued to promote TVT as "the leader in midurethral sling devices" for 'tension-free support for incontinence." [143]Even after Ethicon acknowledged that TVT has never been tension free, the company continued to market it as "Tension-free Support for Incontinence. [144]

Physicians were also not informed in Ethicon's product IFU that tension on the mesh arms decreases effective pore size and interferes with incorporation into tissue. Engineer

[138] Eth.Mesh.00864503.
[139] Eth.Mesh.02625055, Eth.Mesh.02627811, Eth.Mesh.02625375, Eth.Mesh.02625155

[140] Eth.Mesh.06861473.
[141] Eth.Mesh.00161444.
[142] Eth.Mesh.00339437.
[143] Eth.Mesh.00160813 .
[144] Eth.Mesh.00164643; Eth.Mesh.00339053 .

Christophe Vailhe testified that "excessive uniaxial tension on the mesh will decrease the pore size and lead to poor tissue integration." [145]In addition, Mrs. Viahle testified that "excessive tension on the mesh would lead to the decrease in pore size that can lead to poor tissue integration . . . ." [146]Engineer Dan Burkley also testified that once the TVT prolene mesh is either stretched by the surgeon or stretched by in-vivo due to forces in a women's body, it can alter the structure of the pores. [147]

The IFU failed to adequately instruct surgeons on the critical subject of tensioning as repeatedly acknowledged by Ethicon. Ethicon now claims that "tension-free" does not really mean tension-free, but rather, means less tension than as seen in the Burch procedure.[148]Yet, despite its awareness of the problems associated with tensioning, Ethicon failed to revise the conflicting and ambiguous IFU to provide adequate direction on the proper amount of tensioning even though Ethicon was fully aware that improper tensioning could lead to serious complications such as urinary retention, voiding difficulties, de-novo detrusor instability, dyspareunia, vaginal extrusion and urethral erosion.

Ethicon failed to act as a reasonable and prudent medical device manufacturer by failing to inform physicians how to properly tension TVT and that improper tension could affect the pore size of the mesh. These failures by Ethicon have resulted in numerous injuries to patients, including, but not limited to urinary retention, voiding difficulties, de-novo detrusor instability, dyspareunia, and vaginal extrusion and urethral erosion.

[145] Vailhe, 6/20/13, 224:10-226:21
[146] Vailhe, 6/20/13, 224-226
[147] Burkley 5/22/13 430:3-431:10.
[148]Smith 6/4/13 524:20-525:13.

E. **Ethicon did not inform physicians and their patients that Material Safety Data Sheets (MSDSs) for polypropylene resin used to manufacturer polypropylene meshes warned against use of the mesh in a permanently implanted medical device and that studies show that polypropylene causes sarcomas in laboratory rats.**

According to Ethicon Medical Director, Dr. Martin Weisberg, a Material Safety Data Sheet (MSDS) is "a document that discusses the product, the composition, any potential hazards from it . . . Generally, the safety particular of products."[149] As it relates to polypropylene, I have reviewed several MSDSs for polypropylene resin used to manufacturer meshes used in various pelvic floor meshes. All of the MSDSs discussed below are available to the public.

Sunoco, the manufacturer for the polypropylene resin used to manufacture Ethicon's pelvic floor products lists the possibility that polypropylene mesh can cause tumors or cancer. This is documented by the Sunoco MSDS[150] from April 13, 2005 which states in relevant part:

> 15. OTHER INFORMATION
>
> Follow all MSDS/label precautions even after container is emptied because it may retain product residue.
>
> COMPONENT TOXICITY: Polypropylene has been tested in laboratory rats by subcutaneous implantation of discs or powder. Local sarcomas were induced at the implantation site. No epidemiological studies or case report suggest any chronic health hazard from long term exposure of polypropylene decomposition products below the irritation level. (OARC, 19, 128).[151]

Dr. Martin Weisberg, Ethicon Medical Director, is not only familiar with this MSDS, he also has personal experience with it. Dr. Weisberg agrees that the manufacturer of Ethicon's mesh did a study by implanting it under the skin of rats and it did in fact induce sarcomas.[152] Dr. Weisberg also agrees "if there was evidence of cancer-causing abilities of polypropylene . . . a

[149] Weisberg 8/9/13 909:2-9.
[150] Eth.Mesh.02026591-02026595.
[151] Id. at 02026595.
[152] Id. at 930:3-8

reasonable doctor would want to know."[153] And, despite evidence to the contrary in the above MSDS for the resin used to make the polypropylene mesh for TVT, he is not aware of any instance when Ethicon "disclosed to any doctor that there's any evidence that the use of polypropylene mesh might induce sarcomas in its patients."[154]

Dr. David Robinson, a former Ethicon Medical Director, testified that Ethicon never performed any studies or research to determine whether polypropylene could cause cancer in the long term.[155] In addition, he testified that Ethicon never disclosed "the potential that polypropylene in the product could be cancer causing." [156] Dr. Robinson also testified that it would be reasonable for physicians to want to know about polypropylene possibly causing cancer. [157]

Another MSDS from Chevron Phillips[158], a manufacturer of polypropylene resin states:

> MEDICAL APPLICATION CAUTION: Do not use this Chevron Phillips Chemical Company LP material in medical applications involving permanent implantation in the human body or permanent contact with internal body fluids or tissues.
>
> Do not use this Chevron Phillips Chemical Company LP material in medical applications involving brief or temporary implantation in the human body or contact with internal body fluids or tissues unless the material has been provided directly from Chevron Phillips Chemical Company LP under an agreement which expressly acknowledges the contemplated use.
>
> Chevron Phillips Chemical Company LP makes no representation, promise, express warranty or implied warranty concerning the suitability of this material for use in implantation in the human body or in contact with the internal body fluids or tissues.

With respect to the Chevron Phillips MSDS, Ethicon Medical Director, Dr. Martin Weisberg, testified that he did not have the Chevron Phillips MSDS in 2001 when he reviewed

[153] Id. at 951:6-10
[154] Id. at 951:11-16
[155] Robinson (Rough) 9/11/13, 298:18-24
[156] Robinson (Rough) 9/11/13, 306:3-6
[157] Robinson Rough 9/11/13, 306:7-23
[158] Chevron Materials Safety Data Sheet Marlex Polypropylenes (All Grades) Revision Number: 3 (T-3137).

the Sunoco MSDS and no one at Ethicon alerted him to it.[159] If he had been alerted to the Chevron Phillips MSDS, it may have "triggered" an investigation on his part.[160] He also believes that if Ethicon knew about this MSDS, Ethicon should have studied the issue and, if they did not do so, it would have been a violation of the company Credo.[161]

Total Petrochemicals, the polypropylene resin manufacturer for the polypropylene used in AMS' pelvic floor products, Technical Data Sheet for Polypropylene PPR 7220, states in bold red lettering

> "Under no circumstances are any products sold by Total Petrochemicals suitable for human or animal implants." It is further documented that, "The above-mentioned product is NOT in compliance with the US pharmacopoeia because we DID NOT perform required tests." (emphasis from the original document).[162]

The manufacturer of the polypropylene resin for the polypropylene used in competitor pelvic floor products, Phillips Sumika Polypropylene Company, included a similar warning in its MSDS[163]. Specifically, it states:

> "Do not use this Phillips Sumika Polypropylene Company material in medical applications involving permanent implantation in the human body or permanent contact with internal body fluids or tissues. Do not use Phillips Sumika Polypropylene Company material in medical applications involving brief or temporary implantation in the human body or contact with internal body fluids or tissues unless the material has been provided directly from Phillips Sumika Polypropylene Company under an agreement which expressly acknowledges the contemplated use. Phillips Sumika Polypropylene Company makes no representation, promise, express warranty or implied warranty concerning the suitability of this material for the use in implantation in the human body or contact with internal body fluids or tissues."

As discussed above, the possibility that polypropylene mesh can cause tumors or cancer is documented in the Sunoco MSDS, the manufacturer of the polypropylene resin used in the

[159] Weisberg, 8/9/13,944:16-945:5.
[160] Id.
[161] Id. at 947:4-19
[162] Eth.Mesh.02026591
[163] Phillips Sumika Polypropylene Company Material Safety Data Sheet Marlex Polypropylene (All Grades) Revision Number: 5.03 Revision Date: 12/4/2008

TVT Prolene mesh. [164] Specifically, the Sunoco MSDS from April 13, 2005 states: COMPONENT TOXICITY: Polypropylene has been tested in laboratory rats by subcutaneous implantation of discs or powder. Local sarcomas were induced at the implantation site. No epidemiological studies or case report suggest any chronic health hazard from long term exposure of polypropylene decomposition products below the irritation level."[165]

Despite this warning in the MSDS for the polypropylene resin used to manufacture the TVT mesh, there is no evidence that Ethicon informed surgeon about this important information contained in various Manufacturer Safety Data Sheets (MSDS) regarding the use of polypropylene. This information includes the dangers of using polypropylene in a permanent implanted medical device set forth in MSDS that were in the public domain and available to Ethicon if they chose to look. Ethicon also failed to inform physicians that laboratory studies on rats showed that polypropylene caused sarcomas.

The fact that this information has not been disclosed to physicians in any manner (IFUs, direct letters or promotional materials) is especially concerning in light of literature showing reports of cancer associated with polypropylene. Specifically, there have been cases of pseudotumor reported in polypropylene for hernia mesh[166] and inflammatory myofibroplastic tumor of low malignant potential with a TVT device.[167] In addition, there have been 2 cases of bowel cancer associated with mesh used for abdominal sacrocolpopexy, one associated with mersilene and one with polypropylene and TVT placement.[168] A case of primary vaginal

[164] Eth.Mesh.02026591-6595.
[165] Eth.Mesh.02026595.
[166] Karrem, M., Community Oncology, Volume 7/Number 4/April 2010
[167] Kwon S., et al, Female Pelvic Med Recontruct Surg, Volume 18, Number 4, July/August 2012
[168] Ahuja, S., et al, Gynecol Surg (2011) 8:217-221

leiomyosarcoma associated with TVT and anterior repair with Bard Duraderm has also been reported. [169]

Finally, a report of angiosarcoma associated with Darcon vascular grafts was reported in 1999[170] The authors of this article noted at least 8 other sarcomas developing at the site of vascular prosthesis, and that the rate of these sarcoma, associated with foreign bodies, was much higher than the rate of sarcomas in general. All sarcomas associated with Dacron grafts were high grade histology and disseminated at the time of presentation. The authors also describe sarcoma reported at the site of other foreign bodies, such as shrapnel, bullets, steel plates and retained surgical sponges. They also note that the latency period from the acquisition of the foreign body and the development of sarcoma had a mean of 33 years. They document that a chronic foreign body reaction, the same "microscopic foreign body reaction" described by Dr. David Robinson in his Sept 2013 deposition as being clinically insignificant, was the etiology of this carcinogenesis. The authors also describe sacromas developing in rodents after inert plastic polymers were placed in their soft tissue: "The sarcomas developed in rodents in which thick fibrous capsules developed around the implanted material." The authors conclude: "For unknown reasons, the cells in this inflammatory and repair process may undergo a malignant transformation, probably associated with oncogene activation and tumor suppressor gene inactivation. Further studies are warranted to search for the mechanisms involved in foreign body tumorgenesis." To date no manufacturer of mesh products has investigated this oncogenic potential as the authors recommended.

In a report from the International Agency for Research on Cancer: Surgical Implants and Other Foreign Bodies ,"When several polymers were tested in rats according to the same

[169] Moller, K., et al, Gynecologic Oncology 94 (2004) 840-842.
[170] Ben-Izhak, O., et al, Am J Surg Pathology, Issue: Volume 23 (11), 1999, p. 1418

experimental protocol, sarcoma incidences ranged from 70% (polypropylene) to 7% (silicone)".[171] "Polymeric implants prepared as thin smooth films (with the exception of poly(glycolic acid)) are POSSIBLY CARGINOGENIC TO HUMANS"[172]

Given the fact that hernia mesh placement increased in the 1990's with the advent of laparoscopic placement, and that vaginal mesh placed for SUI and POP accelerated in the 2000's, we may be on the cusp of an ever increasing number of foreign body tumors associated with vaginal mesh. To not inform doctors of this significant potential risk, and to not warn patients of an existent risk of cancer, when known, is unconscionable.

Ethicon did not undertake any long term testing to determine whether or not these warnings on the polypropylene resin manufacturers MSDS were associated with long term consequences for permanent human use. This is true despite the fact that Ethicon has knowledge of three of these cancer reports (Kwon, Moller and Ahuja) as they are referenced in Ethicon's 2013 Clinical Evaluation Report regarding TVT.[173]

Additionally, there is no evidence that Ethicon made any effort to inform surgeons of important information contained in various Manufacturer Safety Data Sheets (MSDS) regarding the use of polypropylene. This information includes the dangers of using polypropylene in a permanent implanted medical device. And, that laboratory studies on rats showed that polypropylene caused sarcomas in laboratory rats. Clearly, these facts are critical information relevant to both the surgeon evaluating his or her treatment options and to the patient's informed consent decisions. As a result, Ethicon failed to act like a reasonable and prudent medical device manufacturer.

[171] International Agency for Rsearch on Cancer, Summaries and Evaluations, Vol.:74 (1999).
[172] McGregor, D.B., et al, European Journal of Cancer 36 (2000) 307-313 (emphasis added).
[173] Eth.Mesh.10150515

F. Ethicon did not properly inform physicians and their patients that toxicity testing of the polypropylene mesh revealed that it was cytotoxic or toxic to cells.

Cytotoxicity means toxicity to the cells causing cell injury or death.[174] In a May 26, 2000 Ethicon Memo titled "Review of biocompatibility on the tension-free vaginal tape (TVT) system for compliance to FDA,"[175] the review contains a "Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device" from August 8, 1997. [176] The Cytotoxicity Assessment states "there is some evidence to suggest that the PP [polypropylene] mesh from the sterile Ulmsten device may have cytotoxic potential.[177] In addition, ISO Elution testing "resulted in marked cytotoxicity in tests conducted at Ethicon (Scotland)."

According to former Ethicon Medical Director, Dr. David Robinson, Ethicon never performed "a single long-term study . . . to determine whether or not the Ethicon mesh is clinically cytotoxic in women."[178] In addition, in its IFUs and Patient Brochures, Ethicon never informed physicians or their patients about the possibility of cytotoxicity. [179] Dr. Robison testified that if there is a clinical related outcome related to cytotoxicity, it is reasonable for physicians to want to know that the mesh in the TVT product had been tested multiple times to be severely or marked cytotoxic.[180]

Cytotoxicity can cause death to cells that can lead to an inflammatory response leading to a multitude of injuries, including serious adverse complications such as erosions, chronic pelvic pain, recurrence, worsening incontinence, dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction or the need for additional surgeries.

[174] Robinson 9/11/13 1091:11-21.
[175] Eth.Mesh.06852118-06852129 (5/26/2000 Biocompatibility Review).
[176] Eth.Mesh.06852120 (8/8/1997 Cytotoxicity Risk Assessment).
[177] Id. and Robinson 9/11/13 (rough); 281-288:20.
[178] Robinson,9/11/13 (rough) 293:21-293:11.
[179] Robinson 9/11/13(rough) 305:20-306:2.
[180] Robinson 9/11/13 (rough) 306:24-307:6.

Ethicon did not undertake any long term testing to determine whether the marked cytotoxicty found in the TVT mesh had long term consequences for permanent human use. This is true despite the fact that its own test results showed the mesh to by cytotoxic.

The potential for cytotoxicity or cell death is important information that physicians need to know in order to pass the information on to their patients so that an informed decision can be made about whether to have a permanent medical device implanted in their body. It is clear from Ethicon's Medical Director David Robinson that this information was never passed on to physicians despite the fact that it would have been reasonable for physicians to have this information. As a result, Ethicon did not act as a reasonably prudent medical device manufacturer in it failed to inform physicians and their patients about the risk of its mesh being cytotoxicity.

G. Ethicon's promotional materials sent to physicians related to TVT were inaccurate and failed to reveal material facts about complications and conflict of interests regarding data promoted in the materials.

Since the TVT was first launched, Ethicon has sent materials in various forms to physicians promoting long term follow up data on the original cohort of patients implanted with the TVT from 1995-1996[181]. In addition, the materials tout low complication rates related to various adverse reactions, including erosions. These materials include press releases, marketing brochures and email blasts.

The long term data primarily relied on by Ethicon throughout these materials relates to the Ulmsten/Nillson studies. These studies were originally started by Dr. Ulmsten, the inventor

[181] Eth.Mesh.0015598,; Eth.Mesh.00658058,;Eth.Mesh.01186068; Eth.Mesh.02236784; Eth.Mesh.02237103; Eth.Mesh.03459211; Eth.Mesh. 05183409; Eth.Mesh.00339437,;Eth.Mesh.05794787.

of the TVT, and continued by Dr. Nillson after Dr. Ulmsten's death. Prior to selling the TVT to Johnson & Johnson, Dr. Ulmsten owned a company called Medscand. As discussed more fully below, Johnson & Johnson hired Dr. Ulmsten and Medscand to conduct studies related to the TVT. To this day, Ethicon relies heavily on these studies and uses them in numerous promotional materials despite the fact that Ethicon never disclosed to physicians the potential conflict of interest and inherent bias that exists due to Dr. Ulmsten's relationship with Ethicon and Johnson & Johnson. In addition, Ethicon never disclosed to physicians that the device used in the original Medscand study was different than the TVT device. It is important to physicians using the TVT that the data in these types of promotional materials is accurate, unbiased and that physicians are informed about any potential conflicts of interest in the data contained within the materials. In other words, physicians rely on Ethicon to provide fair and balanced information and to ensure that physician have been given all the data and not just the positive press release data.

Despite using the Ulmsten data to promote the TVT, Ethicon never disclosed to physicians the bias and inherent conflict of interest related to the Ulmsten data. Specifically, in its promotional materials, Ethicon (Johnson and Johnson) never informed physicians about its relationship and contracts with Professor Ulmsten and his company Medscand. It is clear from the contracts that the publications and data from Dr. Ulmsten where contracted for hire by Johnson and Johnson International.[182]

The License and Supply Agreement between Johnson and Johnson International and Medscand (Ulmsten's Company) dated February 13, 1997, states In section 3.6 Milestone

[182] Eth.Mesh.08696085-134.

Payments Johnson and Johnson International (JJI) shall pay shall pay to Medscand the following payments (b). A payment in the amount of $400,000.00 due on February 28, 1997; provided, however, that in the event that Clinical Trials as specified in Exhibit C have not been completed by such date, then such amount shall not be due until the completion of the Clinical Trials.[183]

Under Exhibit F Professor Ulmsten Consulting Agreement with Professor Alf Ivar Ulmsten, under section 4 Confidential Information: Rights to inventions and Copyrights (B) it states any copy rightable work whether published or unpublished created by supplier Dr. Ulmsten directly as a result of or during the performance of services herein shall be considered a work made for hire, to the fullest extent permitted by law and all rights, titles and interest herein, including worldwide copyrights shall be the property of the company as the employer and party specially commissioned said work. [184]

Finally, Exhibit C Clinical Trials, it states the results of clinical trials will be considered acceptable if, first, they do not differ significantly from the results published in the original article published in the Int. Urogynecol J 1996-7:81-86 by U.Ulmsten at et.al., with regards to the following items: Safety 1.1, preoperative complications 1.2 , post operative complications 1 year from operation 2. Efficacy. Second Long term results over 1 year from operation do not show a deterioration of rates significantly different from those of the standard suburethral slingplasties. It is assumed that from 12 – 60 months a gradual decrease in efficacy of 5% is normal. 3. No significant numbers of unexpected i.e. not addressed in the original article published in the Int. Urogynecol J 19967 81-86 by U.Ulmsten at et.al. procedure related i.e. not

[183] Eth.Mesh.08696091.
[184] Eth.Mesh.08696116.

addressed in the review article published in the Int. Urogynecol J 19945: 228-239 by G. N. Ghomiem et.al. complications appear at any time in the postoperative course.[185]

In total, Dr. Ulmsten stood to gain $4.2 million dollars for the 6 papers that he published on the TVT device. In addition, the results of those studies would be found acceptable for payment because they did not differ from the parameters sent by Johnson & Johnson regarding complications and efficacy. The Ulmsten studies have an inherent conflict of interest and bias as they were "made for hire" and standards were set by Johnson & Johnson. As set forth above, if Dr. Ulmsten did not meet the standards set forth by Johnson & Johnson, he did not receive substantial payments for the "studies." As a result of this relationship, there is a clear conflict of interest and potential for enormous bias issues.

The conflict of interest and bias created by the relationship between Ethicon and Dr. Ulmsten was acknowledged by Dr. Axel Arnaud, Ethicon's European Medical Director, in a recent deposition. Specifically, Dr. Arnaud testified that such an agreement like the one discussed above between Dr. Ulmsten and Johnson & Johnson creates a potential conflict of interest. [186] Dr. Arnaud also acknowledged that when Johnson & Johnson enters into this type of agreement with a physician or his company and the study is published, there "certainly" needs to be a disclosure of the relationship. [187]

Additionally, Former Ethicon Medical Director, Dr. David Robinson, testified that in his experience working in the industry for medical device manufacturers, it is best that potential

[185] Eth.Mesh.08696132.
[186] Arnaud 7/20/13 497:24-501:21, 509:8-17.

[187] Arnaud 7/20/13 514:17-515:1.

biases be disclosed. [188] He also testified that if publications from somebody like Ulmsten or Nilsson about safety and efficacy are being published, it is best if they disclose that they have a financial bias or conflict of interest. [189] In fact, in an April 2009 email exchange with Medical Director Piet Hinoul about a physician who, like Ulmsten, is a consultant and inventor for competitor Boston Scientific, Dr. Robinson states that that situation presents "enormous bias issues."[190] Despite two of its medical directors testifying that the relationship between Ulmsten and carried over to Nilsson presents a conflict of interest and bias, Ethicon has never disclosed this information in its promotional pieces. This is information physicians and patients have a right to know so that a proper informed decision regarding the value of the data in the studies and the use of the product can be made.

Aside from never disclosing to physicians the underlying conflict of interest and bias of the Ulmsten studies in its promotional pieces, Ethicon also never informed them about other problems with the data, including incomplete data on the original cohort, data incorrectly reported and erosion rates underreported.

In the original 510k submission for TVT Classic, Ethicon used Medscand data from the Scandinavian Multicenter Study.[191] The report shows that 12 month follow was obtained for 90 of the original 131 patients, without explanation of why there was a loss of 41 patients from the study. The study also describes complication of wound infection: "while the vaginal infection required surgical intervention with resection of exposed mesh". This represents a vaginal mesh erosion/extrusion/ exposure and needs to be reported as such. However, when the paper was published (Ulmsten, Int Urogynecol J 1998), the paper states that there was no defect healing and

[188] Robinson 9/11/2013 214:15-21.
[189] Robinson 9/11/2012 215:8-13.
[190] Eth.Mesh.03259439; Robinson 9/11/13 219:6-220:10.
[191] Eth.Mesh 00371587

no tape rejections. It further misrepresents the outcome for this patient as "The patient with the wound infection had vaginal atrophy. After minimal vaginal wall resection and effective local estrogen treatment she healed without further intervention. There was no tape rejection."

If Ulmsten had reported a mesh erosion/extrusion/exposure with mesh excision in his study, it would not have been acceptable under Exhibit C of his consulting contract for payment of the $400,000.[192] This demonstrates that the results of this paper were potentially biased by the payment Ulmsten would receive for favorable data and should discount the data. At the very least, Ethicon should have informed physicians about the relationship between Ethicon and the Ulmsten studies.

Many of the marketing brochures tout the "[t]he urethral erosion rate less than or equal to that of traditional slings; no reported urethral erosions in 10 studies of 50+ patients.[193] The reference used for the first part of this statement is from Dr. Gary Leach) who looked at traditional sling procedures done before 1993, when traditional slings were performed at the bladder neck and purposely placed under tension to treat severe stress urinary incontinence from intrinsic sphincter deficiency (particularly among Urogynecologists).

The second part of this statement regarding “no uretheral erosions” is incorrect. In published studies, Dr. Karram found one case of urethral erosion in his study of 350 Gynecare TVTs performed (Karram Obstet Gynecol 2003) and Hammad found nine cases of urethral erosion in his study (Hammad Eur Urol 2005).[194] His study followed the complications of 1459 patients 993 of whom had Gynecare TVT, while the remainder has SPARC procedures. While

[192] Eth.Mesh 08696132
[193] Eth.Mesh 00339439
[194] Karram MM, Segal JL, Vassallo BJ and Kleeman SD, “Complications and untoward effects of the tension-free vaginal tape procedure,” Ob & Gyn, 2003 (101:929-32).

the authors do not break down the incidence of urethral erosion by product, it is exceedingly unlikely that all erosions happen in the SPARC group.

The statement regarding “no uretheral erosions” also did not include deTayrac's 2003 paper of 61 patients (31 TVTs) which showed a 3% urethral erosion rate.[195] Dr. Shlomo Raz described a study of 26 patients who presented with voiding dysfunction, including symptoms of severe urethral, pelvic and genital pain, urinary retention, recurrent UTIs, de-novo urgency with urge incontinence found to have mesh from a sling procedure in the bladder or urethra.[196] Their patients were found to have been treated conservatively with anticholinergic medication. They conclude that "dysfunctional voiding symptoms after sling procedure should elicit a high degree of suspicion if pharmacotherapy is not successful in alleviating symptoms...Cystoscopy should be considered if the patient remains symptomatic despite pharmacotherapy".

In one of the Nillson studies, Dr. Nilsson describes four patients on "anticolinergics" (Int Urogynecol J 2008 Table 3). They conclude "It is also encouraging to see that no late adverse effects of the polypropylene tape material was found and that erosion of the tape into adjacent tissue did not occur." However, this statement cannot be made for 4 patients who are on pharmacotherapy without a cystoscopy, which was not performed in the 11 year follow-up study.

Dr. Raz’s review of the literature found mutliple cases of urethral erosions in a large series with TVT. [197] There have also been multiple case reports attesting to the fact that urethral erosion does occur specifically with Gynecare TVT products. [198] To imply that urethal erosion

[195] de Tayrac R, et al, , “A prospective randomized trial comparing tension-free vaginal tape for surgical treatment of stress urinary incontinence,” Am J Obstet Gynecol, 2004 (190:602-8).
[196] Deng DY, Rutman M, Raz S and Rodriguez LV, “Presentation and management of major complications of midurethral slings: Are complications under reported,” Neurourology Urodynamics, , 2007(26:46-52).
[197] *Karram 2003, Hammad 2005*
[198] Sweat, S., et al, “Polypropylene Mesh Tape for Stress Urinary Incontinence: Complication of Urethral Erosion and Outlet Obstruction,” J Urology, 2002 (168:144-146).; ;Gerstenbluth, RE. et al, “Simultaneous Urethral Erosion of Tension-Free Vaginal Tape and Woven Polyester Pubovaginal Sling,” J Urol. 2003(2 Pt 1) (170:525-6); ; ,

does not occur is not giving physicians fair and balance information about the true incidence of urethral erosions with TVT products.

Later, Nilsson publishes the 5 year follow-up of this cohort.[199] He describes the cohort: "a prospective open multicenter trial was conducted in the Nordic countries at the beginning of 1995. The short-term results were published in 1998." This implies that these are the same patients as published in 1998. It is interesting or an incredible coincidence that the exact number of patients receiving 12 months of follow-up in the Medscand publication (90) was the exact number being described in the 5 year study. There is again no mention of the outcome of the other 41 patients from the original cohort. Another interesting detail in the 5 year study is that the original number of centers used for the study (6) was now down to 3, again without explanation. The 5 year report does describe the original patient with the wound infection but again fails to mention she had mesh excised, "1 case (1.1%) of infection of operating site was observed."

In 2006, Dr. Nilsson published a different study on long term outcome of patients with TVT [200]. He describes his new patient population: "A multi-center study comprising only carefully selected primary cases revealed a promising cure rate of 85% after 5 years (reference his 5 year study) and 81% at 7 years."[201] These two papers are the subject of many press releases and marketing brochures, but they never described that these were carefully selected patients. "To our knowledge, the long-term effect and effectiveness of the TVT procedure has not yet been studied in an unselected patient group. We earlier reported 16-month follow-up results of a

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Vassallo, BJ., et al, "Management of latrogenic Vaginal Constriction," Am J Obstet Gynecol, 2003 (102(3):512-20); Haferkamp, A., et al, "Urethral Erosion of Tension-Free Vaginal Tape," J Urol 2002 (167(1): 250).

[199] Ulmsten data; Nilsson Int Urogynecol J 2001.

[200] Kuuva , N, et al. "Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women," Acta Obstetricia Gynecologica Scandanavica 2006(85: 4 482-87)

[201] Nilsson Obstet Gynecol 2004

general patient group referred to a tertiary medical unit and comprising primary, recurrent, mixed, and low pressure urethra cases. In the present study, we report the long-term results in the same above-mentioned group." They describe a 3.1% mesh "visualized" rate, half of which needed surgical resection. These results, more representative of what one would see in a normal practice, is never mentioned in press releases or marketing documents.

Conversely, when Ethicon receives adverse information, it does not make it into the promotional pieces. Dr. AC Wang's abstract, "Tension-Free Vaginal Tape (TVT) for Urinary Stress Incontinence - A Preliminary Report" was used in the original 510k submission in October o f 1997 as support for FDA clearance of the TVT. [202] However, when Dr. Wang reported that he had 25 cases of "failure of vaginal healing considered by him to be potential tape rejection...in each case the revision failed within 2 weeks, requiring further surgery to excise mesh and repair the vaginal wound," this important information never made it into the marketing materials or press releases.[203]

The long-term follow-up data (Ulmsten/Nillson data) used by Ethicon to promote the lack of risk of TVT is spurious at best. We have incomplete data on the original cohort, data that is falsely reported, original sites that were excluded without explanation, and a lead investigator who had a significant relationship and financial incentive to reach certain results with the data. This is the same data which is now used repeatedly in promotional and marketing materials sent to physicians.

[202] Eth.Mesh.00371551
[203] Eth.Mesh.00409675.

H. **Ethicon's Patient Brochures misstate information regarding complications and success rates and lack fair balance.**

In its patient brochures, Ethicon routinely represents to patients and physicians that the success rate of the TVT device is between 97 and 98%. These claims are based on the 5 year, 7 year, and 11 year follow-up to the Ulmsten/Nilsson study. What is not adequately explained to patients is that this "success rate" is a combination of patients who are "cured" and those who are considered "improved," a fact that is not disclosed in advertisements directed at patients, but is generally disclosed in advertisements directed at doctors. Further, Ethicon does not disclose to patients or physicians that the numerous authors of this study on which Ethicon has made the cornerstone of its marketing program are paid consultants of Ethicon, including, Dr. Ulmsten, Dr. Nilsson, Dr. Falconer, and Dr. Rezapour.[204] Ethicon also does not inform patients of the existence of other long-term studies which show a much lower success rate for TVT.

Ethicon's Patient brochures tells patients that 98% of women treated with the Gynecare TVT are still dry or report significantly less leakage after 7 years.[205]This claim is combined with an assertion that the TVT is trusted by over 1 million women. This claim undoubtedly gives women the false impression that this claim of 98% "success" with TVT is based on all of the more than 1 million women who have been treated with TVT, when in fact this statement is based on a single study of 90 patients, only 80 of which were available for follow-up after 7 years.[206] The brochure also does not tell patients that the actual cure rate in this study was only 81.3%. with the TVT until page 7 of the brochure, and then only in fine print at the bottom of the brochure The brochure also does not inform patients of what the criteria for a patient to be

[204] Eth.Mesh.09746615; Eth.Mesh.09748842; Eth.Mesh.09748848; Eth.Mesh.08696050;Eth.Mesh.08167644.
[205] Eth.Mesh .00163583
[206] Nilsson, CG. et. al., "Seven year follow-up of the Tension –Free Vaginal Tape procedure for treatment of urinary incontinence," Ob & Gyn, 2004 (104: S5-S8)

considered "significantly improved" is. Further, patients were not informed that 8% of these 80 patients felt their incontinence had become worse between their 5 year evaluation, and the 7 year evaluation that was the basis of this study. Further Ethicon knew of other studies showing a much lower success rate than the single 90 patient study they had elected to feature in their patient brochures. For example one study found only a 63% success rate after only two years, and that study was sponsored by Ethicon and was a randomized controlled trial (RCT), a study type known to produce the highest quality evidence.[207] Yet Ethicon chose not to share that information with patients. By not presenting patients with an overview of the likely success rates with TVT and instead of selecting a single study which happened to have a high apparent success rate when the "substantially improved" patients were included as a success, Ethicon failed to include fairly balanced material in their brochure.

This same patient brochure also informs women who are considering having TVT surgery that "few women experience complications"[208]. This is a clear misrepresentation of data and complication rates known to Ethicon and the scientific community. For example, in one two-year study, 39% of the patients who received a TVT device experienced a least one complication. In fact, Ethicon's medical director, Dr. Weisberg testified that he knew bladder perforations with TVT occurred in 2 to 3 percent of patients ranging up to 19 percent in some populations.[209] In 2002, Ethicon was also aware of a report of 25 wound healing defects out of a approximately 600 patients – all were suspected to be tape rejections by a very experienced TVT surgeon. This would represent an erosion rate of slightly over 4% seen in these 600 patients.[210] The *Barber* study found an erosion rate in patients receiving the TVT device of between 5 and

[207] Ward K et. al., "Prospective multicentre randomized trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence," BMJ 2002 (325:1-7).
[208] Eth.Mesh 00163583
[209] Weisberg 5/ 31,13422:20-423:1.
[210] Id. at 434:1-437:25; Eth.Mesh.00409674.

6%,[211] a rate consistent with what the President of Ethicon, Renee Selman, believed to be the overall rate of erosions seen with the TVT ("between five and ten percent"). The complication rates known to Ethicon are not consistent with the claim in its patient brochures that few women experience complications, and grossly understate the risk to women deciding whether or not to have the procedure.[212]

Some patient brochures also contain statements and taglines that further give the patient the false impression that complications are rare, and minimize the invasiveness, recovery time and potential complications with the procedure. For example, tag lines like "[s]top oping, tart iving" [213] and "[o]ne day you have stress urinary incontinence, the next day you don't- end of story,"[214] mislead patients into thinking that they will never again have to deal with the symptoms of stress urinary incontinence or other urinary symptoms when the clinical studies show that anywhere between 19% and 37% of patents in clinical studies still have some stress urinary symptoms after treatment with TVT. Further, it minimizes the patients' consideration of the possibility that they may have new symptoms to manage as a result of their operation, including but not limited to potential recurrent urinary tract infections, new urge incontinence, dyspareunia, chronic pain, erosions, and urinary retention.

Other statements in the brochure give women a false impression of the recovery time. "Recovery is quick,"[215]and "Short recovery period and quick return to normal activities,"[216] give patients a false impression of the actual recovery time involved. It is not unusual for women to

[211] Barber et al., "Transobturator tape compared with tension-free vaginal tape for the treatment of stress urinary incontinence," Obstet Gynecol, 2008(111:611-621).
[212] Selman 6/21/13, 583:17-584:17.
[213] Eth.Mesh.08003279.
[214] Eth.Mesh.08003263.
[215] Eth.Mesh.08003291.
[216] Eth.Mesh.08003264.

take 4 weeks or longer before they can safely return to work after the TVT procedure, particularly in jobs that require physical exertion as part of the job functions. Further, the recovery time varies from patient to patient, with some patients taking 8 weeks or even longer to completely heal and return to normal activities.

IV. CONCLUSION

Ethicon has marketed and sold the TVT despite the fact that it is contains numerous characteristics that make it unsuitable for implantation in a woman's vagina. These characteristics include the following: (1) degradation of the mesh; (2) chronic foreign body reaction; (3) fraying and particle loss; (4) Infections and Bio-films; (5) roping and curling of the mesh; (6) loss of pore size with tension; (7) fibrotic bridging leading to scar plate formation and mesh encapsulation; and (8) shrinkage/contraction of the encapsulated mesh.

Not only does Ethicon sell a product which should never be put in the vagina, it failed to inform physicians and their patients about numerous risks associated with the product despite the fact that they knew of all of these risks before the product was launched. This failure by Ethicon has robbed women of their ability to make a proper informed decision with their physician about whether or not to have a permanent medical device implanted into their body. In addition, despite having knowledge to the contrary, Ethicon never told physicians and their patients that the TVT was associated with cancer and could be toxic to their bodies. Finally, while keeping this information from women, Ethicon marketed its product with promotional pieces that did not disclose key conflict of interest information or the true complication rates of its products.

As a result of these failures as fully set forth in this report, the TVT has caused and will continue to cause a multitude of injuries in women, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence,

worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

For the reasons set forth throughout this entire report, Ethicon failed to act like a prudent medical device manufacturer.

All opinions I have are to a reasonable degree of medical certainty. I understand discovery is still ongoing in this case and I reserve my right to amend my opinions if further information is provided in any form including, but not limited to corporate documents, depositions and the expert reports of both Plaintiff and Defense experts.

I declare under penalty of perjury that the foregoing is true and correct.

This 14 day of October 2013

MD

Bruce Rosenzweig, M.D.